

SUPPLEMENTARY INFORMATION

Multicomponent reactions of methyl substituted all-*cis* tetrafluorocyclohexane aldehydes

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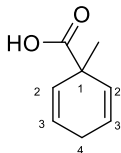
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1. General information

^1H , ^{13}C and ^{19}F NMR spectra were recorded on Bruker Avance or Avance III spectrometers at 500 MHz (^1H NMR), 125 MHz (^{13}C NMR) and 470 MHz (^{19}F NMR). Chemical shifts data were reported as δ in units of parts per million relative to residual solvent and were referenced to the internal solvent, where appropriate. Coupling constants were reported in Hertz (Hz). Analytical thin layer chromatography (TLC) was carried out on Merck silica gel 60 F254 glass-supported plates. Visualisation was by absorption of UV light (λ max 253 or 365 nm), or by thermal development after dipping in an aqueous solution of potassium permanganate, potassium carbonate and sodium hydroxide. Flash column chromatography was carried out on Merck Geduran silica gel 40-63 micron, eluting with solvents as supplied, under a positive pressure of compressed air. Melting points were recorded on an Electrothermal 9100 melting point apparatus and are uncorrected. Electrospray mass spectra were recorded at the University of St Andrews Mass Spectrometry facility on either a Micromass LC TOF spectrometer or a ThermoFisher Orbitrap Excalibur spectrometer from solutions of the analyte in methanol. Additional spectra were obtained at the EPSRC National Mass Spectrometry Service Centre at Swansea using a ThermoFisher Orbitrap LQT XL spectrometer fitted with an ASAP solids probe operating in atmospheric pressure chemical ionisation (APCI) mode.

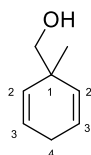
2. Procedure and analytical data

Synthesis of 1-methylcyclohexa-2,5-diene-1-carboxylic acid (**6**)



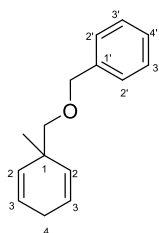
Liquid ammonia (200 mL) was added to benzoic acid **5** (12.2 g, 100 mmol) at -78 °C. Lithium (1.60 g) was then added in small portions until a dark blue colour persisted. After 2 h stirring at the -78 °C, iodomethane (56.1 g, 400 mmol) was added dropwise over a period of 5 min, during which the color gradually changed to yellow and ended up as pale yellow. Ammonia was evaporated, diluted HCl (400 mL) was slowly added and extracted with diethyl ether (200 mL x 3). The combined organic phases were washed with sodium sulfite (200 mL x 2) and water (300 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The resulting pale yellow oil was used without further purification (12.5 g, 91 mmol, 91%); IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 3354 (O-H), 1653 (C=O), 1394 (C-O); ¹H NMR (500 MHz, CDCl₃): δ 5.89-5.85 (2H, m, H-3), 5.32-5.78 (2H, m, H-2), 2.67-2.69 (2H, s, H-4), 1.39 (3H, s, CH₃); ¹³C NMR (101 MHz, CDCl₃): δ 181.3 (COOH), 128.1 (C-3), 125.0 (C-2), 60.5 (C-1), 25.9 (C-4), 14.2 (CH₃).

Synthesis of (1-methylcyclohexa-2,5-dien-1-yl)methanol (**7**)



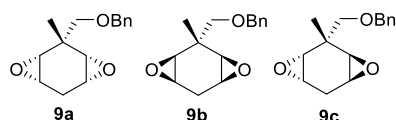
A solution of acid **6** (6.017 g, 48.3 mmol) in THF (80 mL) was added dropwise at -78 °C to a suspension of lithium aluminium hydride (1.9 g, 50 mmol) in THF (160 mL). The reaction mixture was allowed to warm to rt and stirring was continued for 16 h. The reaction was quenched with H₂O (200 mL) and diluted 2M HCl (10 mL). After stirring for another 30 min., the suspension was extracted with EtOAc (100 mL x 3). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure to offer light yellow oil (4.97 g, 40.09 mmol, 83%); IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 3344 (O-H), 3061 (=C-H), 2924 (C-H), 1448 (C-H), 1026 (C-O); ¹H NMR (500 MHz, CDCl₃): δ 5.94-5.90 (2H, m, H-3), 5.49-5.45 (2H, m, H-2), 3.34 (2H, s, CH₂), 2.68-2.66 (2H, m, H-4), 1.02 (3H, s, CH₃); ¹³C NMR (101 MHz, CDCl₃): δ 131.0 (C-3), 126.3 (C-2), 70.9 (C-1), 53.4 (CH₂), 26.5 (C-4), 24.8 (CH₃).

Synthesis of ((1-methylcyclohexa-2,5-dien-1-yl)methoxy)methylbenzene (**8**)



Alcohol (**7**) (2.5 g, 20.16 mmol) was added to a suspension of NaH (0.58 g, 24.19 mmol) in THF (10 mL) at rt. The mixture was stirred for 1 h at room temperature, then benzyl bromide (4.138 g, 24.19 mmol) was added. After overnight stirring, the mixture was quenched with sat. NH_4Cl (50 mL) and extracted with DCM (50 mL x 3). The combined extracts were dried over MgSO_4 , filtered and solvent was removed under reduced pressure. The product was purified by column chromatography (petrol ether/DCM 9.5:0.5 to 9:1) to furnish the ether (**8**) (3.45 g, 16.12 mmol, 80%) as colourless oil; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 3030 (C-H), 2900 (C-H), 1456 (C-C), 1026 (C-O); ^1H NMR (500 MHz, CDCl_3): δ 7.36-7.28 (5H, m, H-2', 3', 4'), 5.80-5.77 (2H, m, H-3), 5.62-5.59 (2H, dt, J = 10.4, 2.0 Hz, H-2), 4.56 (2H, s, Ph- CH_2), 3.25 (2H, s, O- CH_2), 2.68-2.66 (2H, m, H-4), 1.08 (3H, s, CH_3); ^{13}C NMR (126 MHz, CDCl_3): δ 138.8 (C-1'), 132.1 (C-3), 128.3 (C-3'), 127.4 (C-2), 127.3 (C-4'), 123.9 (C-2'), 77.3 (Ph- CH_2), 73.3 (O- CH_2), 37.6 (C-1), 26.5 (C-4), 25.7 (CH_3).

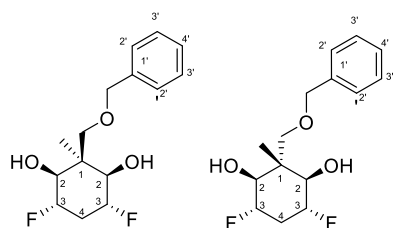
Synthesis of (benzyloxy)methyl-2-methyl-4,8-dioxatricyclooctane (**9a**), (**9b**) and (**9c**):



*m*CPBA (3.363 g, 19.49 mmol) was added to a solution of diene **8** (1.816 g, 8.47 mmol) in CH_2Cl_2 (200 mL) at 0 °C. The reaction mixture was allowed to warm to rt and was stirred for 14 h. The white precipitate was filtered and the filtrate washed with 10% aq. KOH, (100 mL). The aqueous layer was then extracted with DCM (100 mL x 3). The combined organic layers were washed with water (200 mL), dried over Na_2SO_4 , filtered and concentrated under reduced pressure to give a colourless crystalline solid, containing three diastereoisomers of diepoxide (**9a**, **9b** and **9c**) as indicated by ^1H NMR spectrum in a ratio of 6: 4: 1. The product was then purified by silica gel column chromatography (EtOAc/hexane 9.5:0.5, 9:1, 7.5:2.5) to give trans diepoxide **9c** as a colourless oil, (0.1472 g, 0.59 mmol, 7.1%); ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.24 (5H, m, H-2', 3', 4), 4.67-4.55 (2H, m, O- CH_2), 3.58 (1H, d, J = 8.8 Hz, Ph- CH_{2a}), 3.47 (1H, d, J = 8.8 Hz, Ph- CH_{2b}), 3.10 (2H, dddt, J = 8.5, 5.1, 3.3, 1.5 Hz, H-3), 2.85 (2H, ddd, J = 30.5, 6.0, 1.9 Hz, H-2), 2.31 (2H, m, H-4), 1.28 (3H, s, CH_3); followed by a mixture of diastereoisomers **9a** and **9b** as yellow oil (1.042 g, 4.24 mmol, 50%). **9a** (major): ^1H NMR (500 MHz, CDCl_3): δ 7.40-7.28 (5H, m, H-2',

3', 4'), 4.64 (2H, s, O-CH₂), 3.72 (2H, s, Ph-CH₂), 3.16 (2H, ddd, *J* = 4.2, 2.9, 1.3 Hz, H-3), 2.95 (2H, d, *J* = 4.0 Hz, H-2), 2.77 (1H, dt, *J* = 17.2, 1.3 Hz, H-4a), 2.24 (1H, m, H-4b), 1.27 (3H, s, CH₃); **9b** (*minor*): ¹H NMR (500 MHz, CDCl₃): δ 7.40-7.28 (5H, m, H-2', 3', 4'), 4.55 (2H, s, O-CH₂), 3.50 (2H, s, Ph-CH₂), 3.21 (2H, ddd, *J* = 4.1, 2.8, 1.3 Hz, H-3), 2.91 (2H, d, *J* = 3.9 Hz, H-2), 2.69 (1H, dt, *J* = 16.9 Hz, c), 2.21 (1H, m, H-4b), 1.29 (3H, s, CH₃).

Synthesis of (benzyloxy)methyl)-4,6-difluoro-2-methylcyclohexane-1,3-diol, (10a) and (10b):

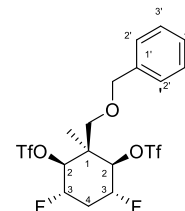


Et₃N.3HF (5.1 g, 31.6 mmol) was added to a mixture of diepoxides **9a** and **9b** (0.974 g, 3.9 mmol) placed in a dry Teflon flask at room temperature. After 12 h stirring at 130 °C, the mixture was cooled to room temperature, poured into NaHCO₃ (20 mL) and extracted with DCM (20 mL x3). The combined organic layers were dried over MgSO₄, filtered, concentrated under reduced pressure to give a 5:4 ratio mixture of 2 diastereomers, **10a** and **10b** (1.37 g, 4.76 mmol) as yellow oil; **10a** (*major*): ¹H NMR (500 MHz, CDCl₃): δ 7.41-7.31 (10H, m, H-2', 3', 4), 4.98 (2H, m, H-3), 4.50 (2H, s, O-CH₂), 3.57 (2H, s, Ph-CH₂), 3.50 (2H, dd, *J* = 15.2, 9.1 Hz, H-2), 2.59 (1H, m, H-4a), 1.73 (1H, m, 2.54, H-4b), 1.22 (3H, s, CH₃); ¹⁹F NMR observe with ¹H decoupling (471 MHz, CDCl₃): δ -183.7 (2F, s, F-3); **(10b)**(*minor*): ¹H NMR (500 MHz, CDCl₃) δ 7.41-7.31 (10H, m, H-2', 3', 4), 4.53(2H, m, H-3), 4.58(2H, s, O-CH₂), 3.80 (2H, dd, *J* = 13.5, 9.3 Hz, H-2), 3.55(2H, s, Ph-CH₂), 2.59(2H, m, H-4a), 1.73 (1H, m, 2.54, H-4b), 0.90.(3H, s, CH₃); ¹⁹F NMR observe with ¹H decoupling (471 MHz, CDCl₃) δ - 190.7 (2F, s, F-3).

Synthesis of (benzyloxy)methyl-4,6-difluoro-2-methylcyclohexane-1,3-diyl bis(trifluoromethanesulfonate), (**11a**, and **11b**)

Trifluoromethanesulfonic anhydride (4.03 g, 14.27 mmol) was slowly added to a mixture of **10a** and **10b** (1.731 g, 6.03 mmol) in pyridine (15 mL, 186 mmol) at 0°C. After 18 h stirring at rt, the reaction mixture was quenched with a mixture of water (50 mL) and CuSO₄ (2 mL) and extracted with diethyl ether (50 mL x

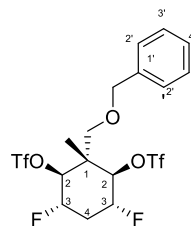
3). The combined organic phases were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The product was purified by means of column chromatography (petroleum ether/DCM 7:3) to offer **11a** (0.998 g, 1.809 mmol, 30%) as white



crystalline solid; M.p. = 87 °C; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1417, 1404 (S=O), 1205 (C-F), 1139 (C-O), 842 (S-O); ¹H NMR (400 MHz, CDCl₃): δ 7.48-7.30 (5H, m, H-2', 3', 4'), 5.46-5.18 (2H, m, H-3), 4.77 (2H, dd, *J* = 13.4, 9.1 Hz, H-2), 4.54 (2H, s, Ph-CH₂), 3.47 (2H, s, O-CH₂), 2.88-2.66 (1H, m, H-4a), 1.96-1.75 (1H, m, H-4b), 1.58 (3H, s, CH₃); ¹³C NMR (126 MHz, CDCl₃): δ 136.1 (C-1'), 128.8 (C-3'), 128.5 (C-2'), 127.8 (C-4'), 118.4 (q, *J* = 319.6 Hz, CF₃), 89.6 (d, *J* = 18.5 Hz, C-2), 85.4 (dd, *J* = 181.1, 14.6 Hz, C-3), 73.9 (O-CH₂), 67.4 (Ph-CH₂), 31.5 (t, *J* = 21.4 Hz, C-4), 29.1 (C-1), 20.1 (CH₃); ¹⁹F NMR observe with ¹H decoupling (376 MHz, CDCl₃): δ -73.3

(6F, d, *J* = 13.4 Hz, OTf), -180.8 (2F, q, *J* = 13.9 Hz, F-3). FTMS (ESI⁺) *m/z* calcd for ([M]+Na) 573.0264; found 573.0247;

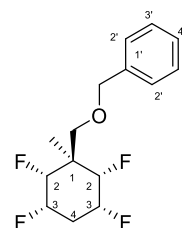
followed by **11b** (0.93 g, 1.688 mmol, 28%) as thick oily liquid; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1415, 1398 (S=O), 1203 (C-F), 1134 (C-O), 927



(S-O); ¹H NMR (400 MHz, CDCl₃): δ 7.52-7.30 (5H, m, H-2', 3', 4'), 5.26 (2H, dd, *J* = 11.4, 9.6 Hz, H-2), 4.95-4.71 (m, 2H, H-3), 4.52 (s, 2H, OCH₂), 3.44 (2H, s, PhCH₂), 2.78-2.86 (1H, m, H -4b), 2.04-1.89 (1H, m, H-4a), 1.03 (3H, s, CH₃); ¹³C NMR (126 MHz, CDCl₃): δ 136.5 (C-1'), 129.0 (C-3'), 128.4 (C- 4'), 128.8 (C-2'), 118.4 (q, *J* = 319.5 Hz, CF₃), 85.3 (dd, *J* = 181.0, 14.6 Hz, C-3), 83.9 (d, *J* = 14.6 Hz, C-2), 73.6 (CH₂), 68.2 (CH₂), 31.5 (t, *J* = 21.7 Hz, C-4), 29.1 (C-1), 22.6 (CH₃); ¹⁹F NMR observe with ¹H decoupling (376 MHz, CDCl₃): δ -73.7 (6F, d, *J* = 12.1 Hz, CF₃), -189.5 (2F, q, *J* = 11.1 Hz, F-3); FTMS (ESI⁺) *m/z* calcd for ([M]+Na) 573.0264; found 573.0252.

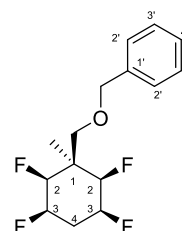
Synthesis of (((2,3,5,6-tetrafluoro-1-methylcyclohexyl)methoxy)methyl)benzene (**12a**)

A mixture of the triflate **11a** (0.7012 g, 1.2 mmol) and Et₃N.3HF (2.68 g, 16 mmol) were placed in Teflon round bottom flask equipped with condenser. After 48 h stirring at 110°C, the mixture was cooled to rt, poured into NaHCO₃ (30 mL) and extracted with dichloromethane (20 mL x 3). Combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure, to give 0.45 g of brown solid. The product was purified by column chromatography (Petroleum ether/ DCM 75:25) to give (**12a**) (0.169 g, 0.58 mmol, 34.8 %) as a white crystalline solid; M.p.= 78 °C; IR: $\nu_{\max}/\text{cm}^{-1}$ 2960, 2891 (C-H), 1130, 1101 (C-O); ¹H NMR (400 MHz, CDCl₃): δ 7.46-7.30 (5H, m, H-2', 3', 4'), 5.07 (2H, m, H-3), 4.75-4.62 (2H, dd, *J*=45.1, 17.0 Hz, H-2), 4.52 (2H, s, O-CH₂), 3.38 (2H, s, Ph-CH₂O), 2.71-2.50 (2H, m, H-4a), 2.12-1.90 (2H, m, H-4b), 1.59 (3H, s, CH₃); ¹³C NMR (101 MHz, CDCl₃): δ 137.2 (C-1'), 128.6 (C-2'), 128.1 (C-4'), 127.7 (C-3') 89.7 (d, *J* = 198.4 Hz, C-3), 87.0 (d, *J* = 180.2 Hz, C-2), 73.6 (CH₂), 71.6 (CH₂), 44.1 (C-1), 27.8 (C-4), 13.9 (CH₃); ¹⁹F{¹H} NMR (471 MHz, CDCl₃): δ -195.2 (2F, AA'XX'), -207.6 (2F, AA'XX', s br, F-3), -206.8 (2F XX' of an AA'XX', s br, F-2); FTMS (ESI⁺) *m/z* calcd for ([M] + Na⁺) 313.119; found 313.1184.



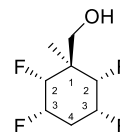
(((2,3,5,6-Tetrafluoro-1-methylcyclohexyl)methoxy)methyl)benzene (**12b**)

Following the analogous method as described in synthesis of **12a**, triflate **11b** (0.3726 g, 0.675 mmol) furnished compound **12b** (0.039 g, 0.135 mmol, 20.4 %) white crystalline solid; M.p = 83 °C; IR: $\nu_{\max}/\text{cm}^{-1}$ 2985, 2891 (C-H), 1558, 1456 (C-C), 1082, 1018 (C-O); ¹H NMR (500 MHz, CDCl₃): δ 7.36 (5H, m, H-2',3',4'), 4.87-4.63 (4H, m, H-2,3), 4.61 (2H,s, Ph-CH₂), 3.72 (2H, s br, O-CH₂), 2.76-2.58 (1H, m, H-4b), 2.41 (1H, dt, *J* = 11.0, 5.3 Hz, H-4b), 1.58 (3H, s, CH₃); ¹³C NR (126 MHz, CDCl₃): δ 138.2 (C-1'), 128.4 (C-2'), 127.7 (C-4'), 127.6 (C-3'), 89.9 (d, *J* = 193.7 Hz, C-2), 85.8 (d, *J* = 185.8 Hz, C-3), 73.6 (Ph-CH₂), 70.8 (O-CH₂), 52.8 (C-1), 27.7 (t, *J* = 22.1 Hz, CH₂), 16.8 (CH₃); ¹⁹F{¹H} NMR (471 MHz, CDCl₃): δ -195.2 (2F, AA'XX'), -207.6 (2F, AA'XX'); FTMS (ESI⁺) *m/z* calcd for ([M] + Na⁺) 313.119; found 313.1182.



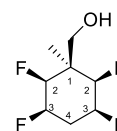
Synthesis of 2,3,5,6-tetrafluoro-1-methylcyclohexyl)methanol (**13a**)

10% of Pd/C (0.02 g) was added to a solution of benzylated alcohol **12a** (0.1696 g, 0.58 mmol) in ethyl acetate (5 mL). The mixture was degased, flushed three times with H₂ and left stirring under H₂ atmosphere at room temperature until completion (TLC monitoring). The reaction mixture was passed through a pad of celite. The filtrate was concentrated and purified using column chromatography (petrol ether/diethyl ether 75:25) resulting in **13a** (0.064 g, 0.319 mmol, 55% yield) as a white crystalline solid; M.p= 68 °C; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 3606 (O-H), 2958, 2891 (C-H), 1045 (C-F); ¹H NMR (500 MHz, CDCl₃): δ 5.06 (2H, dddt, J = 47.5, 13.1, 6.5, 3.1 Hz, H-3), 4.73-4.46 (2H, m, H-2), 3.60 (2H, s, CH₂), 2.66 (1H, dtq, J = 17.1, 11.5, 5.8 Hz, H-4a), 2.08-1.87 (1H, m, H-4b), 1.23 (3H, s, CH₃); ¹³C NMR (101 MHz, CDCl₃): δ 87.8 (d, J = 17.4 Hz, C-2), 86.0 (d, J = 16.9 Hz, C-3), 63.8 (CH₂), 40.8 (C-1), 28.4 (C-4), 15.3 (CH₃); ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -194.1 (2F, **AA'**XX', s br, F-3), -207.7 (2F, **AA'**XX', s br, F-2); (+Cl) m/z calcd for ([M] - H⁺) 199.1662; found 199.1705.



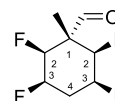
(2,3,5,6-Tetrafluoro-1-methylcyclohexyl)methanol (**13b**)

Following the analogous method as described in synthesis of **13a**, benzylated alcohol **12b** (1.168 g, 0.57 mmol) was used instead of **12a** to furnish **13b** (0.068 g, 0.34 mmol, 59%) as a white crystalline solid; M.p.= 105 °C; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 3300 (O-H), 2956 (C-H); ¹H NMR (400 MHz, CDCl₃): δ 4.92-4.53 (4H, m, H-2, 3), 3.94 (2H, s, CH₂), 2.80-2.60 (1H, m, H-4a), 2.41 (1H, dt, J = 11.1, 5.6 Hz, H-4b), 1.02 (3H, t, J = 1.3 Hz, CH₃); ¹³C NMR (126 MHz, CDCl₃): δ 89.7 (dd, J = 189.7, 15.8 Hz, C-2), 85.7 (d, J = 185.2 Hz, C-3), 63.7 (t, J = 7.7 Hz, CH₂), 29.7 (C-1) 27.7 (t, J = 22.1 Hz, C-4), 16.3 (t, J = 6.3 Hz, CH₃); ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ -195.0 (2F, **AA'**XX'), -208.5 (2F, s br, **AA'**XX'); FTMS (ESI⁻) m/z calcd for ([2M] - H⁺) 399.1570; found 399.1575.

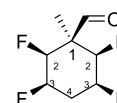


2,3,5,6-Tetrafluoro-1-methylcyclohexane-1-carbaldehyde (14a):

DMSO (10 mL) was added to a mixture of tetrafluoro alcohol (**13a**), (0.134 g, 0.67 mmol) and IBX (1.3 g, 4.67 mmol) at rt. After stirring for 18 h at rt, water was added (30 mL) and extracted with diethyl ether (3 x 60 mL). The combined organic layers were dried over MgSO₄, filtered, concentrated under reduced pressure. Crude product was subjected to column chromatography (petroleum ether/diethyl ether 6:4) to give **14a** (0.1195 g, 0.604 mmol, 90%) as white crystalline solid; M.p = 68-69°C; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1728 (C=O); ¹H NMR (400 MHz, CDCl₃): δ 9.49 (1H, t, *J* = 3.3 Hz, CHO), 5.07 (4H, m, H-2, H-3), 2.65 (1H, m, H-4a), 2.27 (1H, m, H-4b), 1.63 (3H, s, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 198.1 (COH), 90.4 (d, *J* = 205.1 Hz, C-3), 85.2 (d, *J* = 204.6 Hz, C-2), 30.9 (C-1), 27.0 (C-4), 13.3 (CH₃); ¹⁹F NMR{¹H} (376 MHz, CDCl₃): δ -193.3 (4F, **AA'XX'**, s br, F-2, F-3); TOF MS (EI⁺) *m/z* calcd for ([M]) 198.0668; found 198.0671.

**(1*r*,2*R*,3*S*,5*R*,6*S*)-2,3,5,6-tetrafluoro-1-methylcyclohexane-1-carbaldehyde (14b)**

Following analogous method as in synthesis of **14a**, tetrafluoro alcohol (**13b**) was used to furnish **14b** (0.095 g, 0.48 mmol, 68%) as a white crystalline solid; M.p.= 78-79 °C; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1730 (C=O); ¹H NMR (400 MHz, CDCl₃): δ 9.98 (1H, s, CHO), 4.88 (4H, m, H-2, H-3), 2.80 (1H, dtt, *J* = 12.3, 9.2, 3.1 Hz, H-4a), 2.27 (1H, m, H-4b), 1.18 (3H, s br, CH₃); ¹³C NMR (101 MHz, CDCl₃): δ 198.1 (CHO), 90.4 (d, *J* = 179.5 Hz, C-2), 85.3 (d, *J* = 183.8 Hz, C-3), 60.4 (CH₂), 41.3 (C-1), 28.2 (C-4), 15.7 (CH₃); ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ -195.5 (2F, **AA'XX'**, s br, F-3), -205.1 (2F, **AA'XX'**, s br, F-2); FTMS (ESI⁺) *m/z* calcd for ([M]+Na⁺) 221.0565; found 221.0557.

**General procedure A for synthesis of compounds 16-32:**

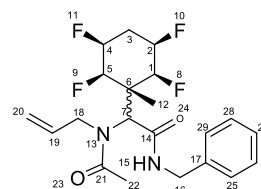
To a solution of the aldehyde (1 equiv.) in DCM was added successively 1.2 equiv. of an appropriate amine (**A1-2**) and 0.1 equiv. of MgSO₄. The resulting mixture was stirred until complete condensation (TLC and ¹H NMR). A solution of the isocyanide (**B1-2**) (1.2 equiv.) in DCM (1 mL) and carboxylic acid (**C1-3**) (1.2 equiv.) in DCM (1 M solution) were added and the resulting solution was allowed to stir at rt for 24 hours. The solvent was evaporated, saturated NH₄Cl (10 mL) was added and the organic layer was extracted into ethyl acetate (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered, concentrated in vacuo and purified by flash chromatography on silica gel and by HPLC.

General procedure B for synthesis of compounds 23, 32:

To a solution of the aldehyde (1 equiv.) in DCM was added successively 1.2 equiv. of an appropriate amine (**A1-2**) and 0.1 equiv. of MgSO_4 . On completion of the condensation (TLC and ^1H NMR), the primary solvent was evaporated and re-dissolved in methanol. A solution of an appropriate isocyanide (**B1-2**) (1.2 equiv.) in methanol, and a solution of carboxylic acid (**C1-3**) (1.2 equiv.) in methanol (1 M solution) were added subsequently and the resulting solution was allowed to stir at rt for 24 hours. On completion, the solvent was evaporated, saturated NH_4Cl (10 mL) was added and the organic layer was extracted into EtOAc (3 x 10 mL). The combined organic extracts were then dried over MgSO_4 , filtered and concentrated in vacuo. The product was purified by flash chromatography on silica gel and if required further by HPLC.

2-(N-Allylacetamido)-N-benzyl-2,3,5,6-tetrafluoro-methylcyclohexyl)acetamide (16)

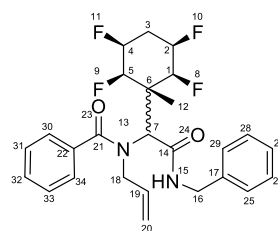
General procedure A with aldehyde **14a** (15 mg, 0.076 mmol) with appropriate components (allylamine, *tert*-butyl isocyanide and acetic acid) gave compound **12** (18 mg, 0.044 mmol, 58%) as white solid after purification using column chromatography (petroleum ether/ EtOAc 9:1, 6:4)



; M.p = 222-223°C; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 3317 (N-H), 1680, 1649 (C=O), 1066 (C-N), 921 (N-H); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 8.27 (1H, s, NH), 7.33 (5H, m, H-25-29), 5.69 (dt, J = 9.8, 7.5, 6.9, Hz, H-19), 5.20- 5.47 (2H, m, H-1, 5), 5.08 (1H, t, J = 1.7 Hz, H-20a), 5.05 (1H, dq, J = 7.2, 1.7 Hz, H-20b), 4.88 (2H, m, H-2, 4), 4.62 (1H, d, J = 17.1 Hz, H-18a), 4.48 (1H, dd, J = 14.6, 6.1 Hz, H-16a), 4.33 (d, J = 10.3 Hz, H-18b), 4.25 (1H, dd, J = 14.6, 5.4 Hz, H-16b), 2.41 (1H, m, H-3a), 2.29 (1H, m, H-3b), 2.15 (3H, s, H-22), 1.55 (3H, s, H-12); ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$): δ 173.5 (C-21), 172.2 (C-14), 149.9 (C-17), 135.1 (C-18), 128.5 (C-25, 29), 128 (C-26, 28), 127.3 (C-27), 114.8 (C-20), 90.1 (dd, J = 185.8, 18.3, Hz, C-1, 5), 86.5 (dd, J = 183.6, 25.6 Hz, C-2, 4), 54.1 (C-7), 53.8 (C-6), 49.3 (C-18), 43.1 (C-16), 26.8 (C-3), 21.6 (C-22), 12.5 (C-12); ^{19}F $\{^1\text{H}\}$ NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$): δ -193.1 (d, J = 14.6 Hz, F-2, 4), -196.1 (dd, J = 13.7, 5.3 Hz, F-1, 5); FTMS (ESI $^-$) m/z calcd for $([\text{M}]-\text{H})$ 413.1852; found 413.1860.

***N*-Allyl-*N*-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)benzamide (17)**

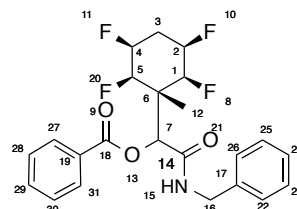
General procedure A. Aldehyde **14a** (0.075 mmol); allylamine, benzyl isocyanide and benzoic acid. Column chromatography (petroleum ether/ EtOAc 8:2) gave **17** (9 mg, 0.019 mmol, 25%) as a white crystalline solid; M.p. = 154-155°C; IR: $\nu_{\max}/\text{cm}^{-1}$ 3323 (N-H), 1726 (C=O), 1687



(C=O), 1244 (C-N), 1020, 970 (C-F); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 7.49-7.21 (10H, m, H-(25-34)), 5.68-5.61 (1H, m, H-19), 5.56-4.51 (7H, m, H-1, 2, 4, 5, 7, 20), 4.42 (1H, dd, $J=14.7, 6.1$ Hz, H-16), 4.35-4.11 (3H, m, H-16b, H-18), 2.84-2.58 (1H, m, H-3a), 2.09-1.83 (1H, m, H-3b), 1.55 (3H, s, H-12); ^{13}C NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$): δ 174.4 (C-14), 168.3 (C-21), 136.9 (C-22), 135.8 (C-17), 133.6 (C-20), 130.2 (C-30, 34), 128.8 (C-31, 33), 128.5, (C-27), 127.9 (C-26, 28), 127.7 (C-32), 126.9 (C-25, 29), 90.0 (d, $J=180.1, 22.2$ Hz, C-1, 5), 86.64 (d, $J=186.7, 20.1$ Hz, C-2, 4), 74.6 (C-7), 48.4 (C-6), 43.7 (C-16), 29.0 (C-3), 12.9 (C-12); ^{19}F $\{^1\text{H}\}$ NMR (376 MHz, $(\text{CD}_3)_2\text{CO}$): δ -193.42 (s br, F-2, 4), -195.99 (s br, F-1, 5); FTMS (ESI^+) m/z calcd for $([\text{M}]+\text{Na}^+)$ 499.1984; found 499.1972; followed by **2-(benzylamino)-2-oxo-**

2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl benzoate

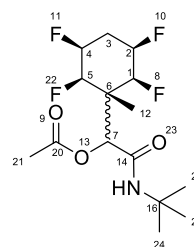
(18): white solid (6 mg, 0.015 mmol, 20%); M.p.= 145-146 °C; IR: $\nu_{\max}/\text{cm}^{-1}$ 3271 (N-H), 2951 (C-H), 1732 (C=O), 1653 (C=O); ^1H NMR (400 MHz, CDCl_3): δ 7.41-7.20 (10H, m, H-



(22-31), 6.57 (1H, s, NH), 5.53 (1H, s, H-7), 5.20- 4.69 (4H, m, H-1, 2, 4, 5), 4.56 (1H, dd, $J=15.0, 6.2$ Hz, H-16a), 4.46 (1H, d, $J=14.9, 5.7$ Hz, H-16b), 2.81-2.61 (1H, m, H-3a), 2.21- 1.95 (1H, m, H-3b), 1.51 (3H, s, H-12); ^{13}C NMR (101 MHz, CDCl_3): δ 167.2 (C-14), 164.8 (C-18), 137.2 (C-17), 134.4 (C-29), 130.0 (C-27, 31), 129.0 (C-28, C-30), 128.9 (C-22, 26), 128.1 (C-19), 127.8 (C-24), 127.5 (C-23, 25), 89.1 (ddd, $J = 190.7, 48.1$ Hz, C-1, 5), 86.0 (dd, $J = 186.3, 31.4$ Hz, C-2, 4), 73.9 (C-7), 46.3 (C-6), 43.4 (C-16), 28.4 (C-3), 12.7 (C-12); ^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3): δ -194.6 (d, $J= 7.8, \text{Hz}$), -194.7 (d, $J = 7.8, \text{Hz}$); FTMS (ESI^+) m/z calcd for $([\text{M}]+\text{Na}^+)$ 460.1512; found 460.1501.

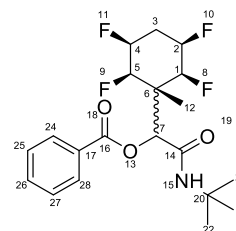
2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl acetate (19)

General procedure A. Aldehyde **14a** (0.05 mmol); allylamine, *tert*-butyl isocyanide and acetic acid. Column chromatography (petroleum ether/ EtOAc 8:2) gave **19** (14 mg, 0.041 mmol, 82%) as yellow solid; M.p. = 169 °C; IR : ν max/cm⁻¹ 3388 (N-H), 2919 (C-H), 1730, 1689 (C=O); ¹H NMR (400 MHz, CDCl₃): δ 5.86 (1H, s, NH), 5.21-4.62 (5H, m, H-1, 2, 4, 5, 7), 2.74 - 2.53 (1H, m, H-3a), 2.24 (3H, s, H-21), 2.23-2.09 (1H, m, H-3b), 1.41 (3H, s, H-12), 1.39 (9H, s, H-24, 25, 26); ¹³C NMR (101 MHz, CDCl₃): δ 168.8 (C-20), 165.8 (C-14), 89.1 (d, J = 190.0 Hz, C-1, 5), 85.9 (d, J =187.1 Hz, C-2, 4), 73.1 (C-7), 52.0 (C-16), 45.6 (C-6), 29.7 (C-3), 28.6 (C-24, 25, 26), 22.7, 20.8 (C-21), 12.9 (C-12); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.0 (s br , F-2, 4) , -194.4 (dd, J = 13.7, 6.9 Hz, F-1, 5); FTMS (ESI⁺) m/z calcd for ([M]+Na) 364.1511; found 364.1495.



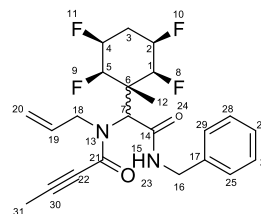
(*R*)-2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl benzoate (20)

General procedure A. Aldehyde **14a** (0.05 mmol), allylamine, *tert*-butyl isocyanide and benzoic acid. Column chromatography (petroleum ether/ EtOAc 7:3) gave **20** (16 mg, 0.04 mmol, 79%) as white solid; M.p.= 178°C; IR : ν max/cm⁻¹ 3307 (N-H), 1653 (C=O), 1066 (C-N), 948 (N-H); ¹H NMR (400 MHz, CDCl₃): δ 8.22-7.48 (5H, m, H-(24- 28)), 6.02 (1H, s, NH), 5.29 (1H, s, H-7), 5.26- 4.70 (4H, m, H-1, 2, 4, 5), 2.68 (1H, m, H-3a), 2.21 (1H, m, H-3b), 1.51 (3H, s, H-12), 1.36 (9H, s, H-21-23); ¹³C NMR (101 MHz, CDCl₃): δ 166.0 (C-16), 164.5 (C-14), 134.4 (C-26), 129.8 (C-24, 28), 129.1 (C-27), 89.1 (d, J = 190.0 Hz, C-1,5), 85.9 (d, J = 185.5 Hz, C-2,4), 73.5 (C-6), 52.0 (C-20), 28.5 (C-21, 22, 23), 28.1 (C-3), 12.9 (C-5); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.2 (s br, -194.6 (dd, J = 13.4, 7.2 Hz); FTMS (ESI⁺) m/z calcd for ([M]+Na⁺) 426.1668; found 426.1653.

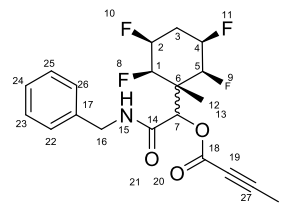


***N*-allyl-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexylethylbutynamide (21)**

General procedure A. Aldehyde **14a** (0.05 mmol), allylamine, benzyl isocyanide and 2-butynoic acid. Column chromatography (petroleum ether/ EtOAc 7:3) gave **21** (5 mg, 0.011 mmol, 22 %) as white solid; M.p. = 198 °C; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 3307 (N-H), 3067, 2990 (C-H), 1690 (C=O), 1587

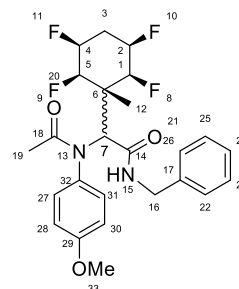


(C-C); ^1H NMR (400 MHz, CDCl_3): δ 7.42-7.29 (5H, m, C- 25-29), 6.39 (1H, s br, NH), 5.81-5.68 (1H, m, C-19), 5.18- 5.11 (2H, m, H-20), 5.09- 4.79 (4H, m, H-1, 2, 4, 5), 4.49 (1H, dd, J = 14.7, 6.2 Hz, H-16a), 4.45-4.35 (3H, m, H-7, H-18), 4.15 (1H, dd, J = 14.8, 4.9 Hz, H-16b), 2.63 (1H, s (br), H-3a), 2.11 -2.01 (1H, m, 3b), 2.01 (3H, s, H-31), 1.48 (1H, s, H-12); ^{13}C NMR (101 MHz, CDCl_3): δ 182.2 (C-14), 157.3 (C-21), 133.5 (C-19), 128.9 (C-26, 28), 128.7, 128.5 (C-17), 127.9 (C-25, 29), 127.7 (C-27), 117.9 (C-20), 92.8 (C-30), 89.9 (dd, J = 185.5, 32.7, Hz, C-1, 5), 84.3 (dd, J = 188.8, 31.1 Hz, C-2, 4), 73.3 (C-22), 64.8 (C-7), 48.4 (C-18), 43.8 (C-16), 29.7 (C-6), 23.4 (C-3), 12.8 (C-12), 4.0 (C-31); ^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3): δ -193.07 (s br), -195.93 (s br); FTMS (ESI^+) m/z calcd for $([\text{M}]+\text{Na})$ 461.1828; found 461.1809; followed by **2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexylethyl but-2-ynoate (22)** (6 mg, 0.015 mmol, 30%) as white solid; M.p. = 147 °C; IR : $\nu_{\text{max}}/\text{cm}^{-1}$ 3550 (N-H), 1680, 1653 (C=O), 1558 (C-C); ^1H NMR (400 MHz, CDCl_3): δ 7.44- 7.28 (5H, m, H- 22-26), 6.51 (1H, s, NH), 5.27 (1H, s, H-7), 5.16 -4.62 (4H, m, H-1, 2, 4, 5), 4.51 (2H, dd, J = 30.1, 5.8 Hz, H-16), 2.66 (1H, m, H-3a), 2.00-2.09 (1H, m, H-3b), 1.59 (3H, s, H-28), 1.43 (3H, t, J = 1.6 Hz, H-12); ^{13}C NMR (101 MHz, CDCl_3): δ 166.3 (C-14), 151.5 (C-18), 137.1 (C-17), 128.9 (C-23, 25), 127.9 (C-24), 127.7 (C-22, 26), 89.1 (dd, J = 189.1, 15.0 Hz, C-1). 88.5 (dd, J = 189.5, 16.7 Hz, C-5), 85.9 (dd, J = 186.6, 8.5 Hz, C-2, 4), 74.1 (C-27), 71.0 (C-19), 60.4 (C-7), 43.5 (C-16), 28.2 (C-3), 23.8 (C-6), 12.4 (C-12), 4.1 (C-28); ^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3): δ -194.49 (d, J = 7.3 Hz, F-2, 4), -194.53 (d, J = 7.3 Hz, F-1, 5); FTMS (ESI^+) m/z calcd for $([\text{M}]+\text{H})$ 400.1535; found 400.1517.

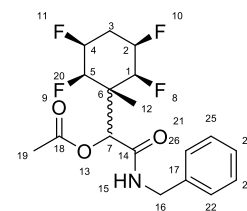


Benzyl-2-((4-methoxyphenyl)acetamido)-2,3,5,6-tetrafluoro-1-methylcyclohexyl)acetamide (23)

General procedure A. Aldehyde **14a** (0.05 mmol), *p*-anisidine, benzyl isocyanide and acetic acid. Column chromatography (petroleum ether/ EtOAc 8:2) gave **23** (6 mg, 0.0125 mmol, 25%) as orange solid; M.p. = 47 °C; IR : $\nu_{\max}/\text{cm}^{-1}$ 3332 (N-H), 2924 (C-H), 1745, 1662 (C=O), 1529(C-C); ^1H NMR (400 MHz, CDCl_3): δ 7.43- 7.30 (5H, m, H- 22-25), 7.02- 6.93 (4H, m



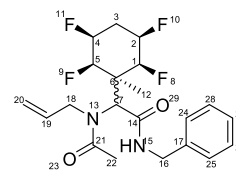
, H-27, 28, 30, 31), 5.27 - 4.78 (5H, m, H-1, 2, 4, 5, 7), 4.48 (2H, d, J = 5.8 Hz, H-16), 3.84 (1H, m, H-3a), 2.62 (1H, s, H-3b), 1.87 (3H, s, H-19), 1.37 (1H, s, H-12); ^{13}C NMR (101 MHz, CDCl_3): δ 174.6 (C-18), 168.5 (C-14), 159.6 (C-29), 137.6 (C-17), 135.7 (C-32) 128.9 (C-22, 26), 128.0 (C-23, 25), 127.8 (C-24), 114.8 (C-28, 30), 114.5 (C-27, 31), 87.4-84.8 (m, C-1, 2, 4, 5), 56.6 (C-7), 55.4 (C-34), 46.5 (C-6), 126.1 (C-32), 43.8 (C-16), 27.7 (C-3) 24.1 (C-19), 13.2 (C-12); ^{19}F { ^1H } NMR (376 MHz, CDCl_3): δ -193.9 (2F, AA'XX'), -194.1 (s br, AA'XX'); FTMS (ESI $^+$) m/z calcd for ([M]+Na) 503.1933; found 503.1925; followed by **2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl acetate (24)** (7 mg, 0.018 mmol, 37 %) as orange oil; IR: $\nu_{\max}/\text{cm}^{-1}$ 3337 (N-H), 2922, 2851 (C-H), 1747, 1668 (C=O); ^1H NMR (400 MHz, CDCl_3): δ 7.44-7.30 (5H, m, H- 22-26), 6.43 (1H, s br, NH), 5.23 (1H, s, H-7), 5.15-4.64 (4H, m, H-1, 2, 4, 5), 4.54 (1H, dd, J = 14.8, 5.9 Hz, H-16a), 4.46 (1H, dd, J = 14.7, 5.8 Hz, H-16b), 2.74-2.57 (1H, m, H-3a), 2.22 (3H, s, H-19), 2.17-2.03 (1H, m, H-3b), 1.40 (3H, J = 1.6 Hz, H-12); ^{13}C NMR (101 MHz, CDCl_3): δ 173.4 (C-14), 169.0 (C-18), 137.1 (C-17), 128.9 (C-22, 26), 128.0 (C-24), 127.7 (C-23, 25), 89.2 (d, J = 188.1, 26.0 Hz, C-1, 5), 86.9 (d, J = 174, 22.7 Hz, C-2, 4), 73.3 (C-7), 45.5 (C-6), 43.5 (C-16), 29.6 (C-3), 20.8 (C-19), 12.5 (C-12); ^{19}F { ^1H } NMR (376 MHz, CDCl_3): δ -194.52 (d, J = 7.5 Hz, F-2, 4), -194.56 (d, J = 7.4 Hz, F-1, 5); FTMS (ESI $^+$) m/z calcd for ([M]+Na) 398.1355; found 398.1345.



General procedure B. Aldehyde **14a** (0.025 mmol with **A2**, **B1** and **C1** after purification furnished **23** (5 mg, 0.013 mmol, 53%).

2-(*N*-Allylacetamido)-*N*-benzyl-2,3,5,6-tetrafluoro-1-methylcyclohexyl)acetamide (25)

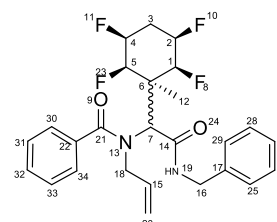
General procedure A. Aldehyde **14b** (0.05 mmol), allylamine, benzyl isocyanide and acetic acid. Chromatography (petroleum ether/ EtOAc 6: 4) gave **25** (15 mg, 0.036 mmol, 72%) as a white solid; M.p.= 138-139 °C; IR : ν max/cm⁻¹ 3203 (N-H),



1668 (C=O), 1627 (C=O), 1012 (C-N); ¹H NMR (400 MHz, CDCl₃): δ 7.40- 7.27 (5H, m, H- 24-28), 6.83 (1H, s br, NH), 5.86-5.69 (1H, m, H-19), 5.23 (2H, d, *J* = 10.8 Hz, H-20), 5.17- 4.53 (5H, H-1,2,4,5,7), 4.48 (2H, dd, *J* = 14.8, 5.9 Hz, H-16a), 4.35 (1H, dd, *J* = 14.7, 5.9 Hz, 2H), 4.30 (1H, d, *J* = 17.6 Hz, H-18a), 4.08-3.98 (1H, m, H-18b), 2.74-2.57 (1H, m, 3a), 2.48 - 2.35 (1H, m, H-3b), 2.22 (3H, s, H-22), 1.25 (3H, s, H-12); ¹³C NMR (101 MHz, CDCl₃): δ 173.2 (C-21), 168.3 (C-14), 137.6 (C-17), 133.2 (C-20), 128.7(C-24, 25) , 127.7 (C-26, 28), 127.6 (C-27), 110.0 (C-19), 90.09 (dd, *J* = 189.0 Hz, 21.8, C-3, 4), 85.53 (dd, *J* = 182.4, 47.9 Hz, C-1, 5), 67.0 (C-7), 45.9 (C-18), 45.1 (C-6), 43.6 (C-16), 27.3 (C-3), 22.9 (C-22), 15.3 (C-12); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.5 (s br, F-2), -195.6 (s br, F-4), -202.1 (dd, *J* = 26.9, 14.0 Hz, F-1), -206.3 (s br, F-5); FTMS (ESI⁺) *m/z* calcd for ([M]+H) 415.2008; found 415.1988.

***N*-allyl-*N*-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)benzamide (26)**

General procedure A. Aldehyde **14b** (0.063 mmol), allylamine, benzyl isocyanide and benzoic acid. Column chromatography (petroleum ether/ EtOAc 7:3) gave **26** (24 mg, 0.050 mmol, 80 %) as white solid; M.p. = 196-197 °C; IR : ν max/cm⁻¹ 3259 (N-H), 1734 (C=O), 1668 (C=O), 1012



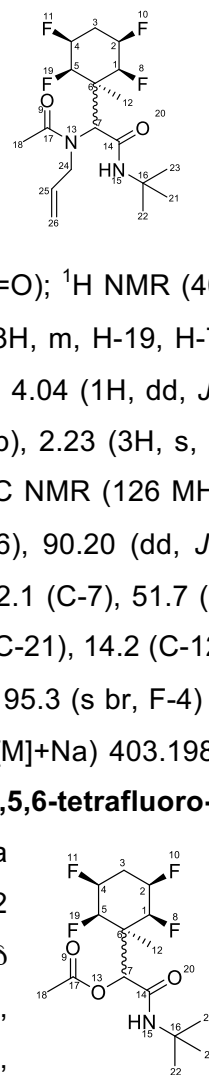
(C-N); ¹H NMR (400 MHz, CDCl₃): δ 7.56- 7.30 (10H, m, H- 25-34), 5.65- 5.57 (1H, m, H-15), 4.6-4.42 (7H, m, H-1, 2, 4, 5, 7, 20), 4.54 (1H, dd, *J* = 14.8, 5.8 Hz, H-16a), 4.46 (1H, dd, *J* = 14.8, 5.6 Hz, H-16b), 4.29 (1H, dd, *J* = 15.6, 5.2 Hz, H-18a), 4.05- 3.34 (1H, m, H-18b), 2.78- 2.59 (1H, m, H-3a), 2.52- 2.40 (1H, m, H-3b), 1.33 (3 H, s, H-12); ¹³C NMR (126 MHz, CDCl₃): δ 176.9 (C-21), 172.9 (C-14), 135.7 (C-17), 130.6 (C-22), 128.8 (C-26, 28, 31, 33), 127.8 (C-27, 32), 127.6 (C-19) 126.8 (C-25, 29, 30, 34), 110.0 (C-20), 90.1 (d, *J* = 180.3 Hz, C-2, 4), 85.7 (d, *J* = 167.1 Hz, C-1, 5), 61.0 (C-7), 45.4 (C-6), 43.6 (C-16), 27.3 (C-3), 16.1 (C-12); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.3 (dd, *J* = 13.6, 4.4 Hz, F-2), -195.3 (s br, F-4) , -202.1 (s br, F-3) , - 205.7 (s br, F-5); FTMS (ESI⁺) *m/z* calcd for ([M]+H) 477.2165; found 477.2146.

2-(*N*-allylacetamido)-*N*-(*tert*-butyl)-2,3,5,6-tetrafluoro-1-methylcyclohexyl)acetamide (27)

Following general procedure A using 0.05 mmol. of tetrafluoro aldehyde **14b** with an appropriate components (allylamine, *tert*-butyl isocyanide and acetic acid) after the purification using column chromatography (petroleum ether/ EtOAc 8:2) furnished **27** (5 mg, 0.013 mmol, 26%) as a white solid; M.p. = 146-147 °C;

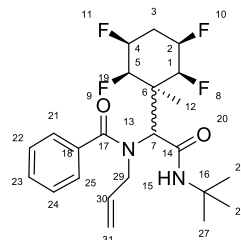
IR : ν max/cm⁻¹ 3367 (N-H), 3240 (C-H), 1749 (C=O), 1654 (C=O); ¹H NMR (400 MHz, CDCl₃): δ 6.42 (1H, s, NH), 5.83 (1H, s, H-15), 5.35-5.21 (3H, m, H-19, H-7), 5.20-4.50 (4H, m, H-1, 2, 4, 5), 4.40 (1H, d, *J* = 17.3 Hz, H-17a), 4.04 (1H, dd, *J* = 17.4, 6.0 Hz, H-17b), 2.77-2.53 (1H, m, H-3a), 2.41 (1H, m, H-3b), 2.23 (3H, s, H-21), 1.35 (9H, s, H-24, 25, 26), 1.23 (3H, t, *J* = 1.3 Hz, H-12); ¹³C NMR (126 MHz, CDCl₃): δ 173.6 (C-17), 167.8 (C-14), 133.6 (C-25), 117.9 (C-26), 90.20 (dd, *J* = 190.7, 21.0 Hz, C-1, 5), 85.56 (dd, *J* = 178.5, 21.5 Hz, C-2, 4), 62.1 (C-7), 51.7 (C-16), 45.8 (C-6), 32.0 (C-17), 28.5 (C-24, 25, 26), 27.3 (C-3), 22.9 (C-21), 14.2 (C-12); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.41 (d, *J* = 4.4 Hz, F-2), -195.3 (s br, F-4), -202.1 (s br, F-1), -206.3 (s br, F-5); FTMS (ESI⁺) *m/z* calcd for([M]+Na) 403.1985; found 403.1971; followed by **2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl) EtOAc (28)** (6 mg, 0.021 mmol, 41%) as a

white solid; M.p. = 161 °C; IR : ν max/cm⁻¹ 3408 (N-H), 2976, 2932 (C-H), 1746 (C=O), 1668 (C=O); ¹H NMR (400 MHz, CDCl₃): δ 5.86 (1H, s, NH), 5.28 (1H, d, *J* = 1.1 Hz, H-7), 4.96- 4.61 (4H, m, H-1,2,4,5), 2.76-2.58 (1H, m, H-3a), 2.45 (1H, dt, *J* = 10.8, 5.1 Hz, H-3b), 2.20 (3H, s, H-18), 1.40 (9H, s, H-21, 22, 23), 1.07 (3H, s, H-12); ¹³C NMR (101 MHz CDCl₃): δ 169.7 (C-16), 165.5 (C-14), 90.2 (dd, *J* = 173.1, 21.0 Hz, C-1), 88.3 (dd, *J* = 182.0, 21.3 Hz, C-2), 86.5- 84.1 (m, C-4, 5), 71.2 (C-7), 52.0 (C-20), 43.8 (C-6) 28.6 (C-21, 22, 23), 27.6 (C-3), 20.6 (C-17), 13.5 (C-12); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -195.2 (dd, *J* = 13.9, 4.4 Hz), -195.4 (dd, *J* = 12.8, 4.5 Hz), -204.2 (dd, *J* = 22.0, 12.3 Hz), -207.6 (dd, *J* = 22.1, 13.9 Hz); FTMS (ESI⁺) *m/z* calcd for ([M]+Na) 364.1511; found 364.1496.

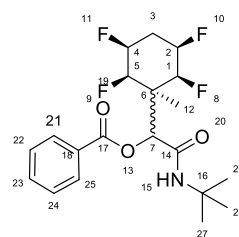


***N*-allyl-*N*-2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)benzamide (**29**)**

General procedure A. Aldehyde **14b** (0.05 mmol), allylamine, *tert*-butyl isocyanide and benzoic acid. Column chromatography (petroleum ether/ EtOAc 6:4) gave **29** (4 mg, 0.0091 mmol, 18%) as a white solid; M.p. = 194 °C; IR : ν max/cm⁻¹ 3309 (N-H), 2902, 2850 (C-H), 1434 (C=O), 1672 (C=O), 1631 (C=C); ¹H NMR (400 MHz, CDCl₃): δ 7.50-7.35 (5H, m, H- 21-25), 7.02

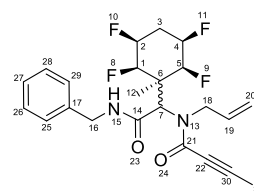


(1H, s br), NH), 5.73 (1H, m, H-30), 5.18 (3H, m, H-7, H-31), 4.85 (4H, m, H-1, 2, 4, 5), 4.33 (1H, dd, *J* = 15.7, 4.9 Hz, H-29a), 4.00 (1H, m, H- 29b), 2.66 (1H, m, H-3a), 2.44 (1H, m, H-3b), 1.40 (9H, s, H-26, 27, 28), 1.34 (3H, s, H-12); ¹³C NMR (126 MHz, CDCl₃): δ 183.8 (C-14), 174.7 (C-17), 136.0 (C-18), 132.6 (C-30), 130.5 (C-23), 128.7 (C-22, 24), 126.7 (C-21, 25), 119.8 (C-31), 90.2 (dd, *J*= 189.3, 21.8 Hz, C-2,4), 85.5 (d, *J* = 183.5, 46.0 Hz, C-1,5), 73.5 (C-7) 51.7 (C-16), 45.9 (C-6), 29.7 (C-29), 28.6 (C-(26-28)), 27.3 (C-3), 16.0 (C-12); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.3 (dd, *J* = 13.5, 4.2 Hz), -195.2 (s br) , -202.4 (s br) , -205.6 (s br); FTMS (ESI⁺) *m/z* calcd for([M]+Na) 465.2141; found 465.2125; followed by **2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl benzoate (30)** (5 mg, 0.012 mmol, 25%) as a white solid; M.p.= 214-215 °C ; IR : ν max/cm⁻¹ 3424 (N-H), 2915, 2851 (C-H), 1718 (C=O), 1684 (C=O); ¹H NMR (400 MHz, CDCl₃): δ 8.16-8.00 (2H, m, H- 21, 25), 7.71-7.58 (1H, m, H-23), 7.56-7.44 (1H, m, H-22, 24), 5.99 (1H, s, NH), 5.58 (1H, d, *J* = 1.1 Hz, H-7), 5.09-4.61 (4H, m, 1, 2, 4, 5), 2.85 -2.63 (1H, m, H-3a), 2.47 (1H, m, H-3b), 1.41 (9H, s, H- 26-28), 1.23 (3H, t, *J* = 1.3 Hz, H-12); ¹³C NMR (101 MHz, CDCl₃): δ 165.2 (C-14), 165.1 (C-17), 133.8 (C-23), 130.4 (C-18), 129.8 (C-21, 25), 128.6 (C-22, 24), 90.35 (d, *J* = 167.9, 19.7 Hz, C-1, 5), 85.39 (dd, *J* = 182.6, 21.9 Hz, C-2,-4). 71.4 (C-7), 51.7 (C-16), 44.6 (C-6), 28.6 (C-26, 27, 28), 27.3 (C-3), 13.7 (C-12); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -195.1 (dd, *J* = 13.9, 4.6 Hz), -195.4 (dd, *J* = 12.7, 4.4 Hz), -204.3 (dd, *J* = 22.4, 12.5 Hz), -207.0 (dd, *J* = 22.4, 14.1 Hz); FTMS (ESI⁺) *m/z* calcd for([M]+Na) 426.1668; found 426.1652.



***N*-allyl-*N*-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexylethylbut-2-ynamide (**31**)**

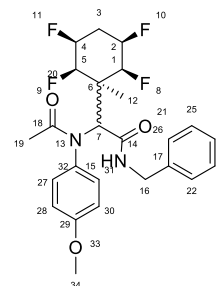
General procedure A. Aldehyde **14b** (0.05 mmol), allylamine, benzyl isocyanide and 2-butyric acid. Column chromatography (petroleum ether/ EtOAc 6:4) gave **31** (10 mg, 0.22 mmol, 46%) as a white solid; M.p. = 161 °C; IR : ν max/cm⁻¹ 3350 (N-H), 2914, 2850 (C-H), 2239 (C≡C)



1735 (C=O), 1627 (C=C); ¹H NMR (400 MHz, CDCl₃): δ 7.42- 7.27 (5H, m, H- 25-29), 6.69 (1H, s, NH), 5.91-5.78 (1H, m, H-19), 5.43-5.08 (3H, m, H-7, 20), 5.06- 4.54 (4H, m, H-1, 2, 4, 5), 4.49 (1H, dd, *J* = 14.8, 5.8 Hz, H-16a), (dd, *J* = 14.9, 5.5 Hz, H-16b), 4.30-3.97 (2H, m, H-18), 2.73-2.56 (1H, m, H-3a), 2.41 (dt, *J* = 10.8, 5.2 Hz, H-3b), 2.06 (3H, s, H-31), 1.24 (3H, s, H-12); ¹³C NMR (101 MHz CDCl₃): δ 167.8 (C-14), 156.8 (C-21), 137.6 (C-17), 132.8 (C-19), 128.7 (C-26, 28), 127.7 (C-27), 127.5 (C-25, 29), 117.8 (C-20), 91.9 (C-30), 90.0 (d, *J* = 188.9, 20.3 Hz, C- 1, 5), 85.5 (d, *J* = 184.1, 34.5 Hz C-2, 4), 73.5 (C-22), 61.8 (C-7), 48.0 (C-18), 43.6 (C-16), 29.2 (C-6), 27.3 (C-3), 15.6 (C-12), 4.18 (C-31); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.4 (d, *J* = 13.9, Hz), -195.4 (d, *J* = 11.5, Hz), -201.5 (s br), -206.7 (dd, *J* = 25.7, 12.8, Hz); FTMS (ESI⁺) *m/z* calcd for ([M]+Na) 461.1828; found 461.1814.

***N*-benzyl-2-(*N*-(4-methoxyphenyl)acetamido)-2,3,5,6-tetrafluoro-1-methylcyclohexylacetamide (**32**)**

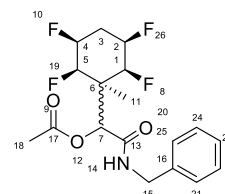
General procedure B. Aldehyde **14a** (0.05 mmol), *p*-anisidine, benzyl isocyanide and acetic acid. Column chromatography (petroleum ether/ EtOAc 8:2) gave **32** (11 mg, 0.0229 mmol, 46%) as white solid; M.p. = 167 °C; IR : ν max/cm⁻¹ 3296(N-H), 2922 (C-H), 1647 (C=O); ¹H NMR (400 MHz, CDCl₃): δ 7.39-7.29 (5H, m, H- 22-26), 6.89-6.78 (4H, m, H-27, 28, 30, 31),



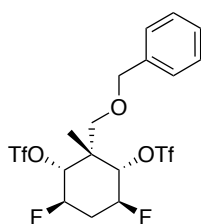
6.25 (1H, s br, NH), 5.18-4.60 (4H, m, H-1, 2, 4, 5), 4.49 (1H, dd, *J* = 14.0, 6.4, H-16a), 4.45-4.33 (2H, m, H-7, 16b), 3.78 (3H, s, H-34), 2.76-2.62 (1H, m H-3a), 2.53-2.38 (1H, m, H-3b), 1.28 (3H, s, H-19), 1.02 (3H, s, H-12); ¹³C NMR (101 MHz CDCl₃): δ 174.5 (C-18), 170.3 (C-14), 154.1 (C-29), 141.3 (C-32), 137.3 (C-17), 128.8 (C-22, 26), 127.7 (C-24), 127.6 (C-23, 25), 118.5 (C-27, 31), 114.8 (C-28, 30), 90.8 (dd, *J* = 185.5, 20.0 Hz C-1, 5), 85.6 (dd, *J* = 185.1, 27.9 Hz, C-2, 4), 60.5 (C-7), 55.7 (C-34), 43.8 (C-16), 43.3 (C-6), 29.7 (C-19), 27.3 (C-3), 13.0 (C-12); ¹⁹F observe with ¹H decoupling NMR (376 MHz, CDCl₃): δ -194.7 (dd, *J* = 14.9, 4.2 Hz), -195.4

(dd, $J = 12.6, 4.2$ Hz), -203.8 (dd, $J = 24.2, 12.5$ Hz), -205.0 (dd, $J = 24.1, 14.8$ Hz); FTMS (ESI⁺) m/z calcd for ([M]+Na) 503.1933; found 503.1916.

General procedure A. Aldehyde **14b** (0.05 mmol), *p*-anisidine, benzyl isocyanide and acetic acid. Chromatography gave **32** (by ¹⁹F NMR) and **2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexylethyl acetate (33)** (8 mg, 0.021 mmol, 43 %) as yellow oil; IR : $\nu_{\text{max}}/\text{cm}^{-1}$ 3265 (N-H), 2922 (C-H), 1700, 1683 (C=O), 1018 (C-O); ¹H NMR (400 MHz, CDCl₃): δ 7.49-7.29 (5H, m, H- 20-24), 6.89-4.61 (5H, m, H-1,2,4,5,7), 4.58 (1H, dd, $J = 14.6, 6.1$ Hz, H-15a), 4.51 (1H, dd, $J = 14.5, 5.9$ Hz, H-15b), 2.80-2.53 (1H, m, H-3a), 2.50- 2.34 (1H, m, H-3b), 1.90 (3H, s, H-18), 0.73 (3H, t, $J = 1.3$ Hz, H-12); ¹³C NMR (126 MHz CDCl₃): δ 171.5 (C-13), 170.4 (C-17), 137.5 (C-16), 128.9 (C- 21, 25), 127.9 (C-23), 127.8 (C-22, 24), 89.7 (dd, $J = 182.6, 27.5$ Hz, C-1, 5), 85.7 (dd, $J = 171.9, 27.0$ Hz, C-2, 4), 68.9 (C-7), 43.6 (C-15), 31.9 (C-6), 29.7 (C-18), 27.5 (C-3), 12.5 (C-11); ¹⁹F {¹H} NMR (376 MHz, CDCl₃): δ -194.7 (dd, $J = 14.0, 4.1$ Hz), -195.2 (dd, $J = 13.0, 4.0$ Hz), -205.6 (dd, $J = 22.1, 13.0$ Hz), -208.2 (dd, $J = 22.1, 13.8$ Hz); FTMS (ESI⁺) m/z calcd for ([M]+Na) 398.1355; found 398.1343.

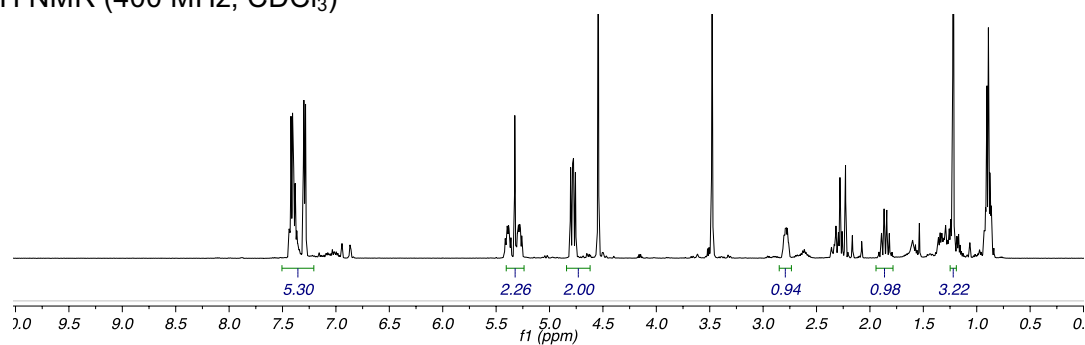


3. ^1H , ^{13}C and ^{19}F NMR spectra

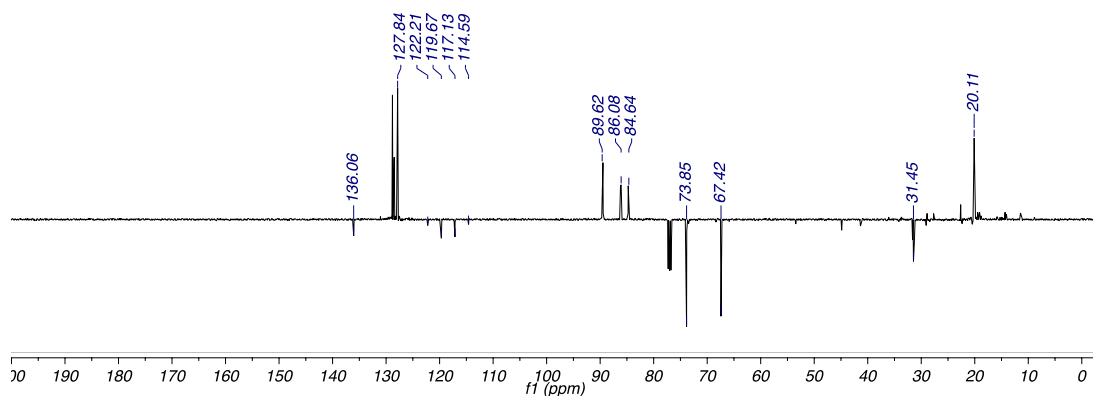


11.a: (Benzyloxy)methyl-4,6-difluoro-2-methylcyclohexane-1,3-diyl bis(trifluoromethanesulfonate)

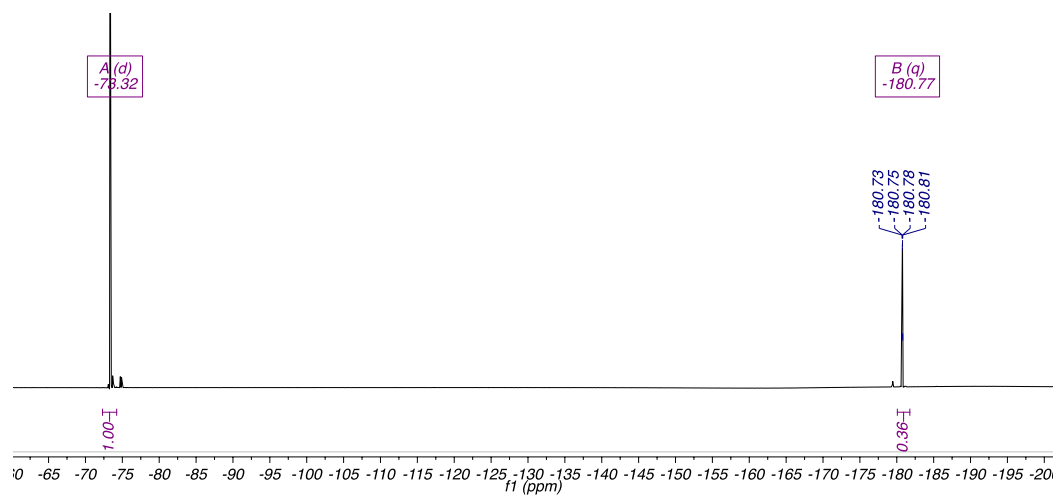
^1H NMR (400 MHz, CDCl_3)

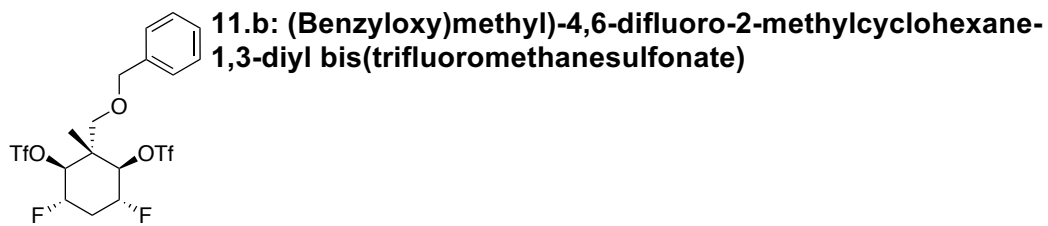


^{13}C NMR (126 MHz, CDCl_3)

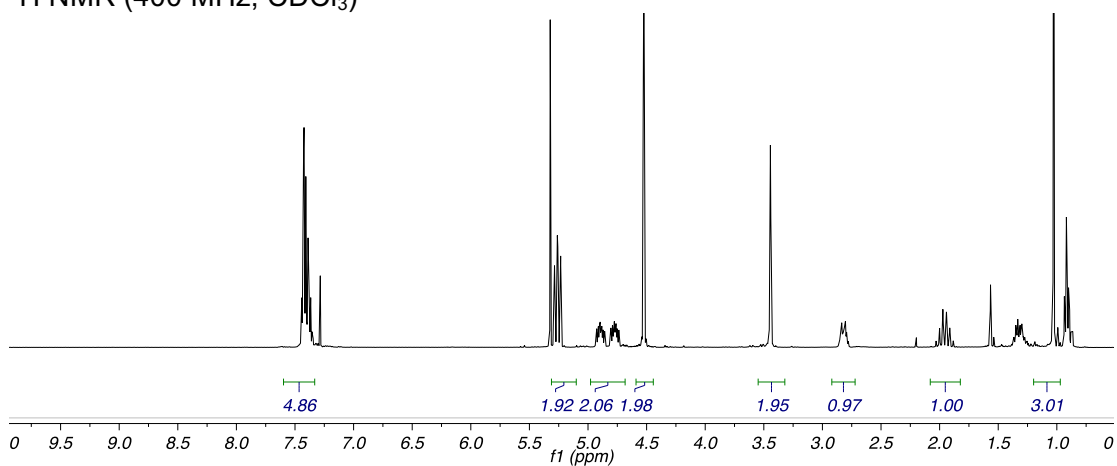


^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)

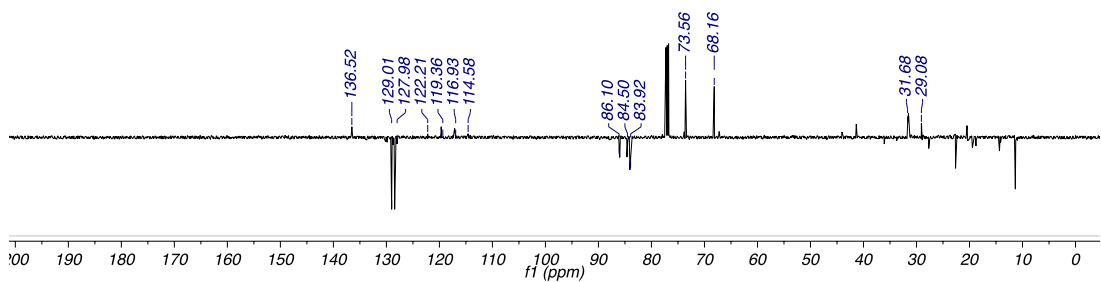




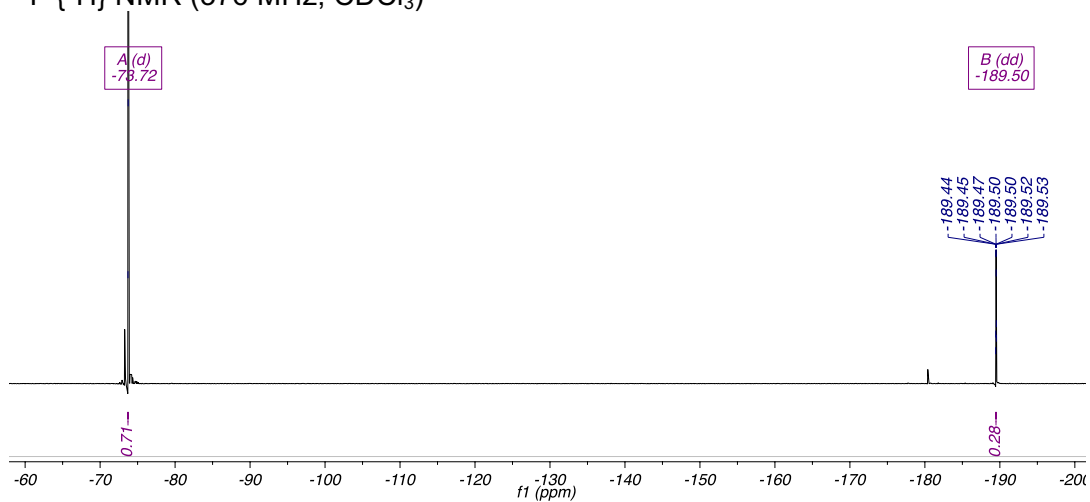
^1H NMR (400 MHz, CDCl_3)

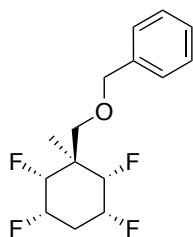


^{13}C NMR (126 MHz, CDCl_3)



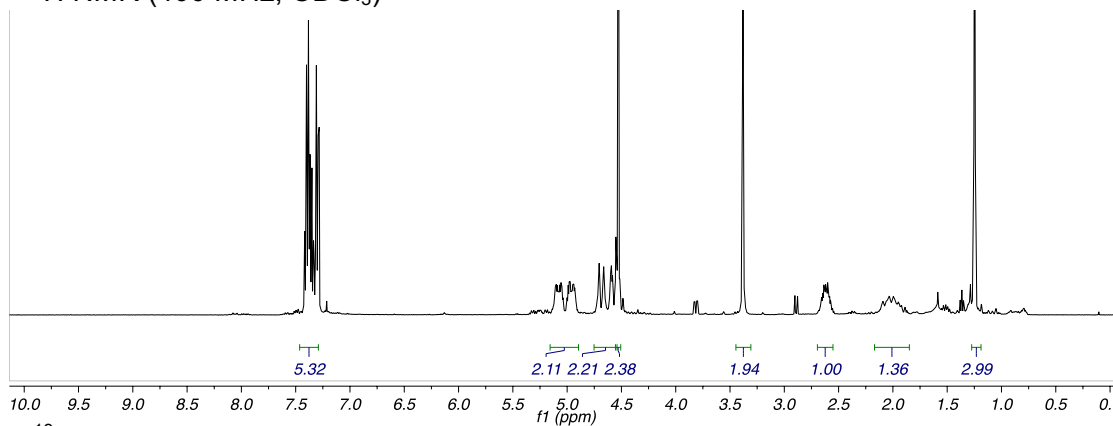
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



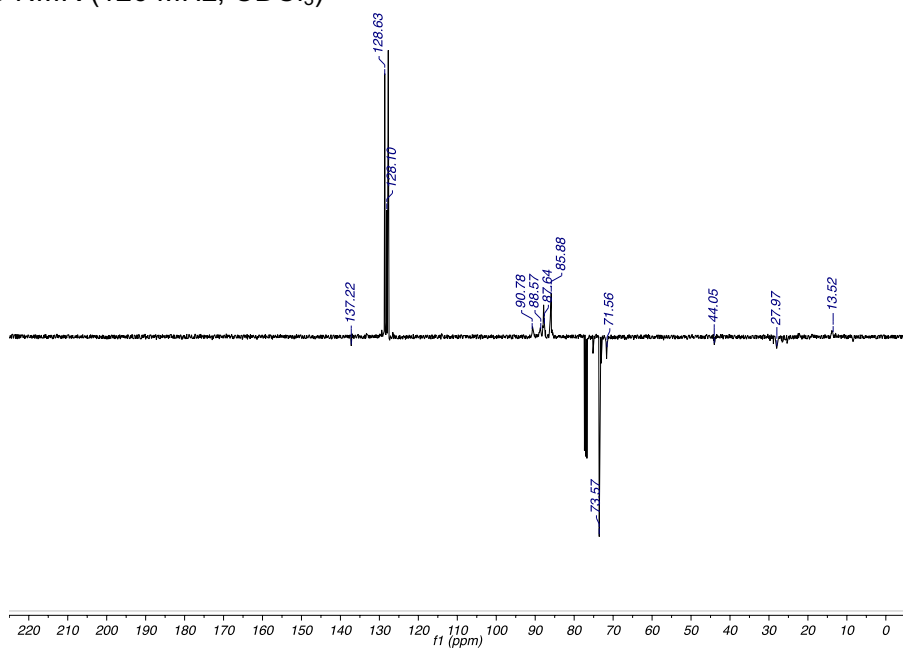


12a: (((2,3,5,6-Tetrafluoro-1-methylcyclohexyl)methoxy)methyl)benzene

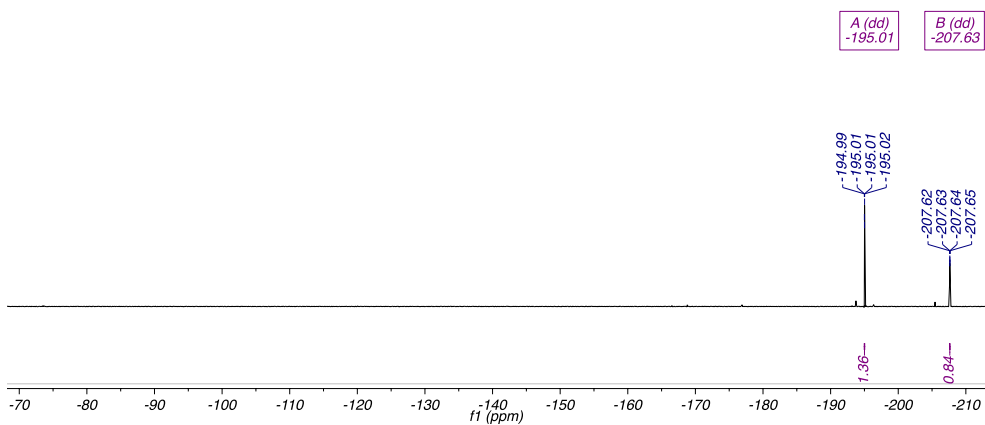
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)



^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)

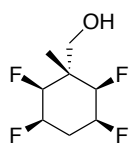




¹³C NMR (125 MHz, CDCl₃)

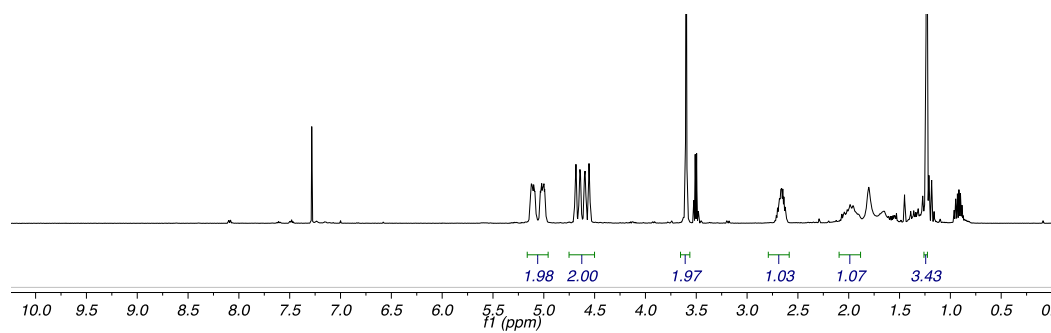
138.03, 128.41, 127.73, 127.56, 90.46, 88.93, 86.62, 84.87, 73.58, 70.73, 52.83, 27.67, 16.78

^{13}C NMR spectrum (570 MHz, CDCl_3) of compound 1. The spectrum shows two main signals: a doublet (dd) at approximately -195 ppm (labeled B (dd)) and a doublet (dd) at approximately -207 ppm (labeled A (dd)). The chemical shifts for the peaks are: -194.99, -195.01, -195.07, -195.02 ppm for signal B, and -207.62, -207.63, -207.64, -207.65 ppm for signal A. The integration values are 1.47 for signal B and 1.00 for signal A.

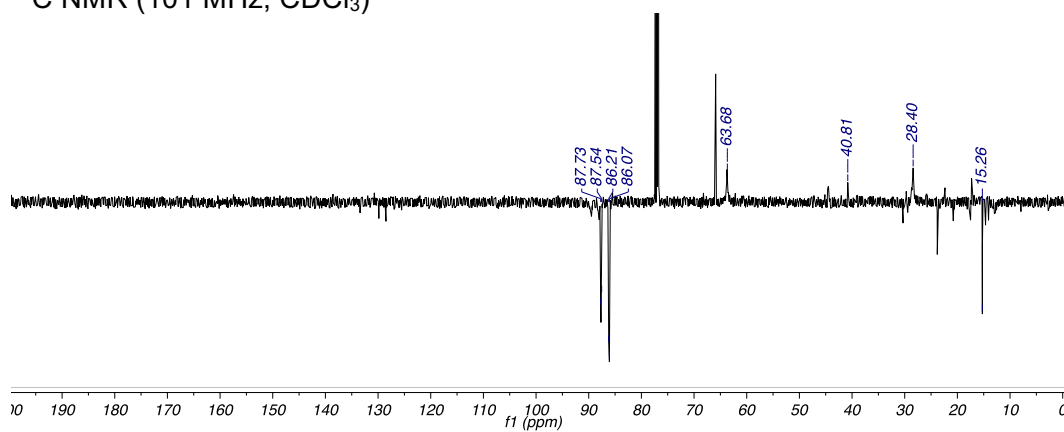


13a: 2,3,5,6-Tetrafluoro-1-methylcyclohexyl)methanol

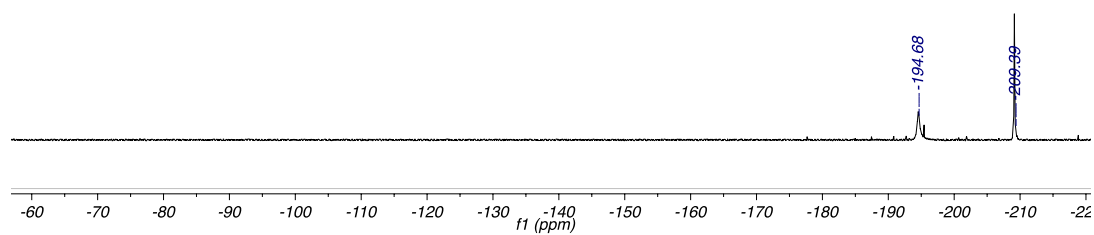
^1H NMR (500 MHz, CDCl_3)

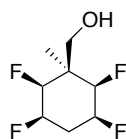


^{13}C NMR (101 MHz, CDCl_3)



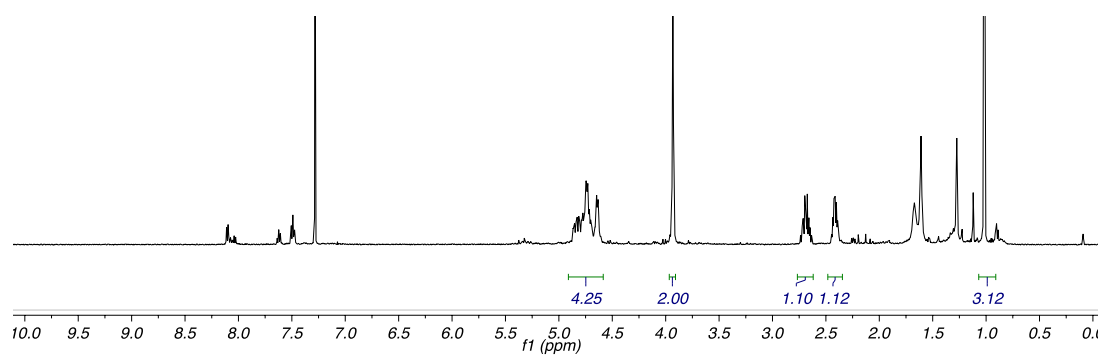
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



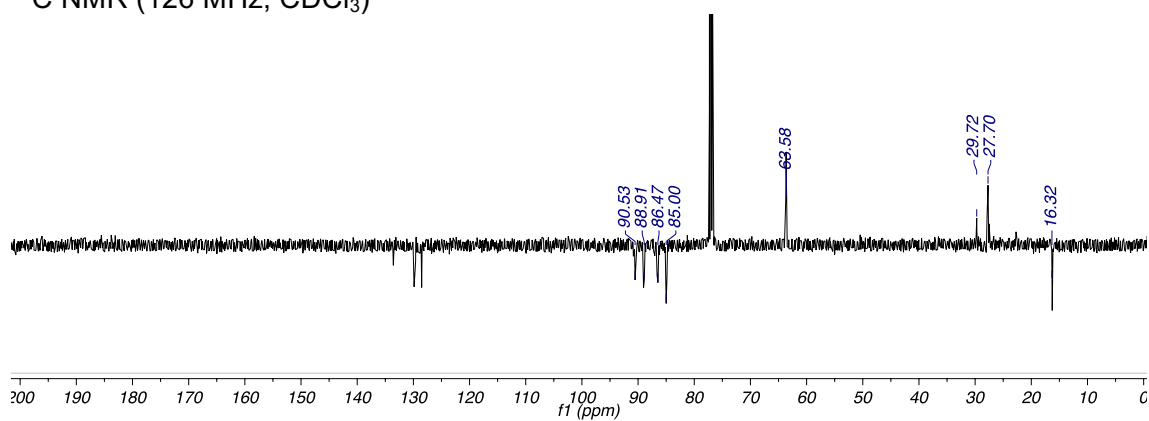


13b: 2,3,5,6-Tetrafluoro-1-methylcyclohexylmethanol

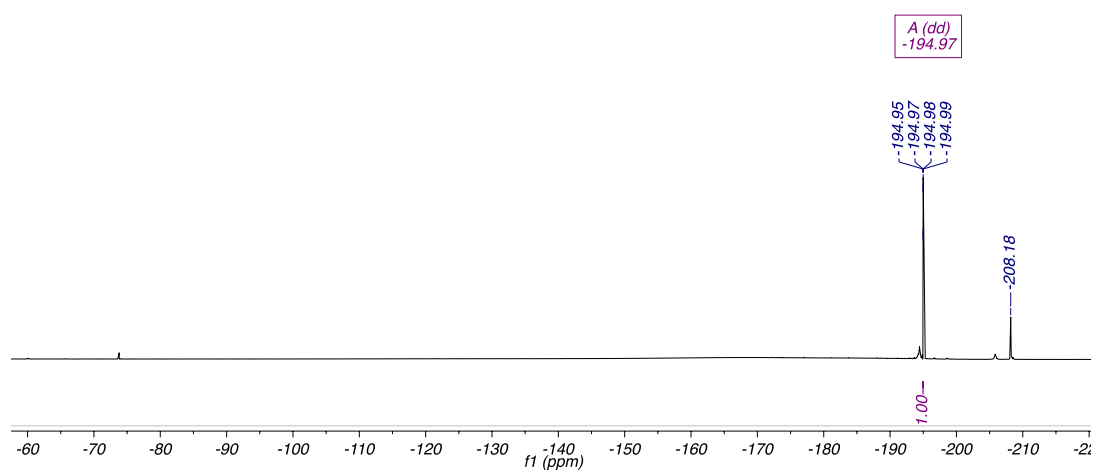
^1H NMR (400 MHz, CDCl_3)

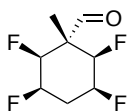


^{13}C NMR (126 MHz, CDCl_3)



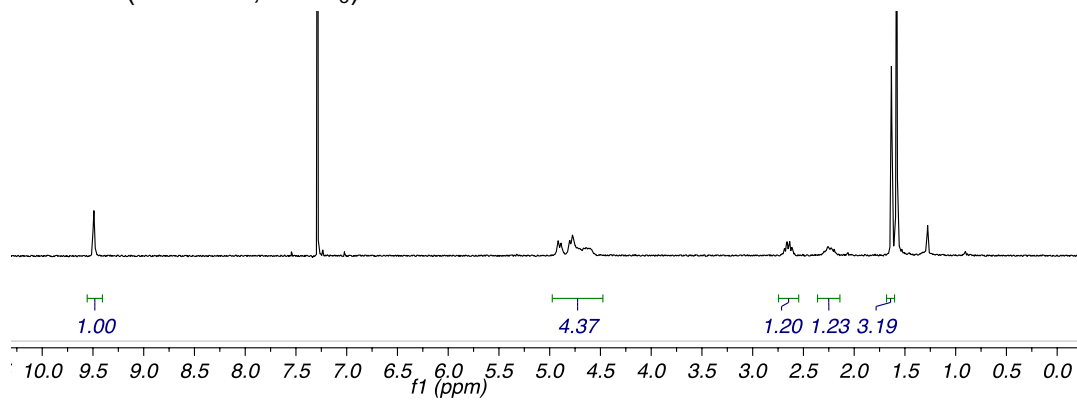
^{19}F { ^1H } NMR (376 MHz, CDCl_3)



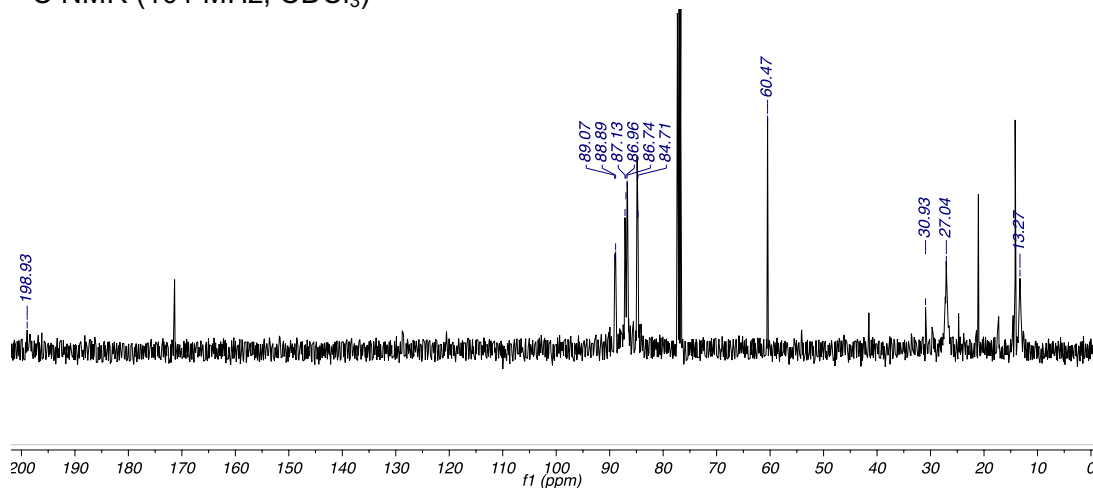


14a: 2,3,5,6-Tetrafluoro-1-methylcyclohexane-1-carbaldehyde

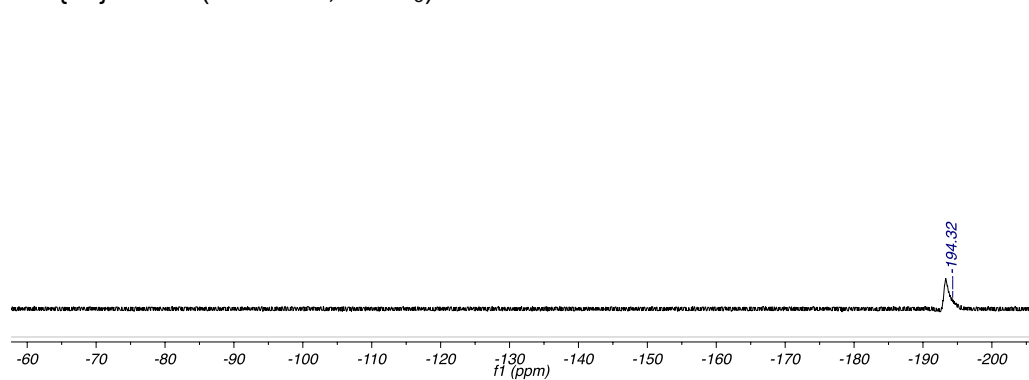
^1H NMR (400 MHz, CDCl_3)

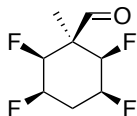


^{13}C NMR (101 MHz, CDCl_3)



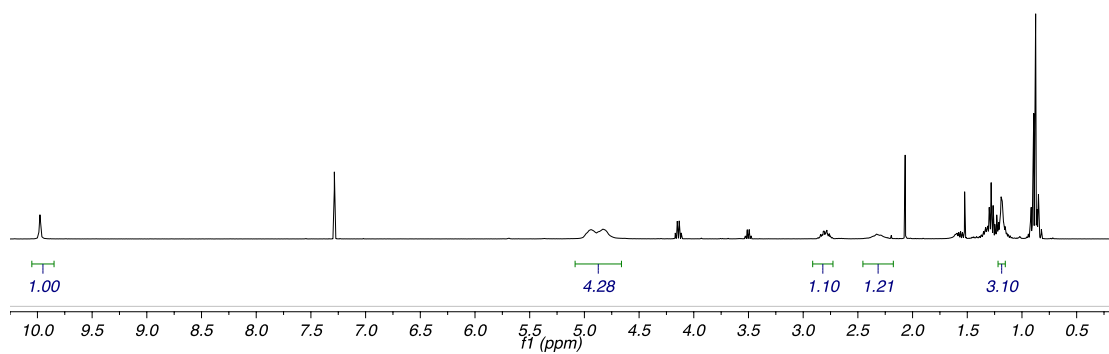
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



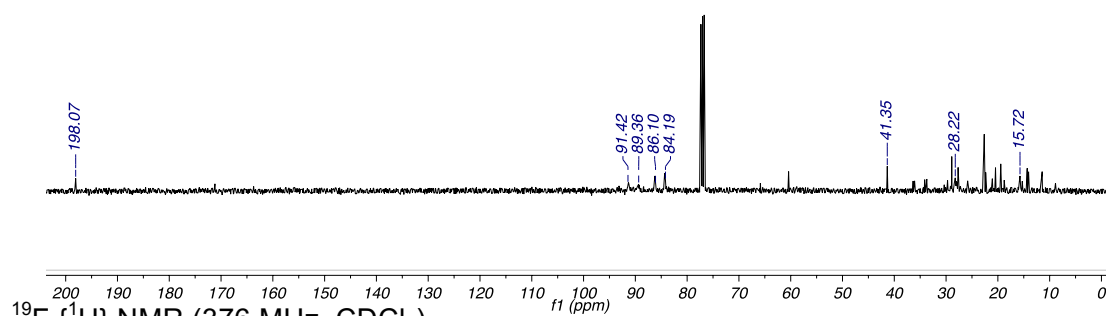


14b: 2,3,5,6-Tetrafluoro-1-methylcyclohexane-1-carbaldehyde

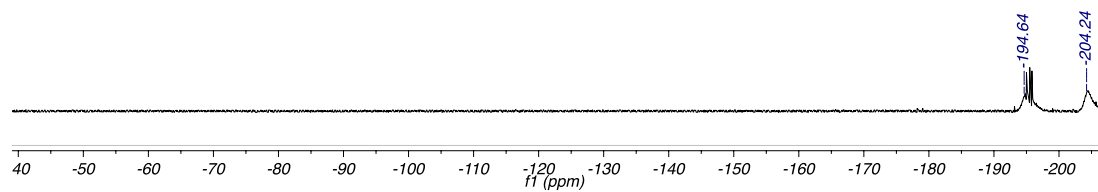
^1H NMR (400 MHz, CDCl_3)

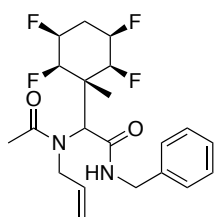


^{13}C NMR (101 MHz, CDCl_3)



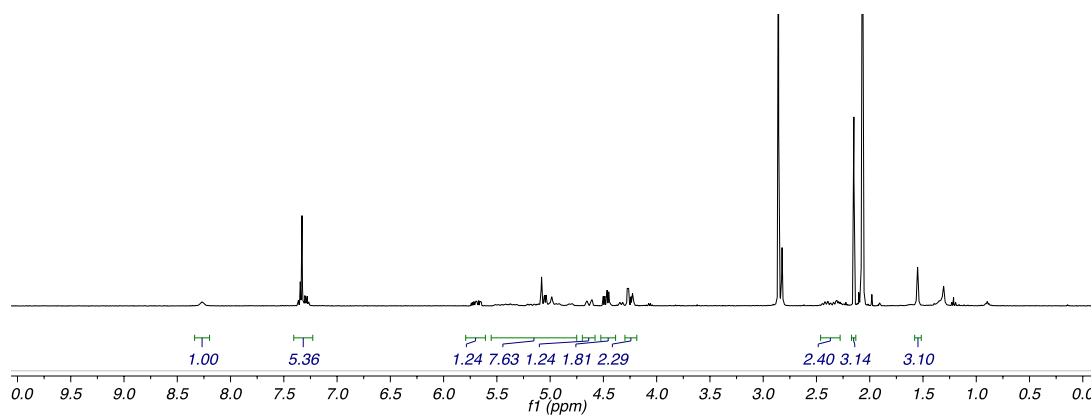
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



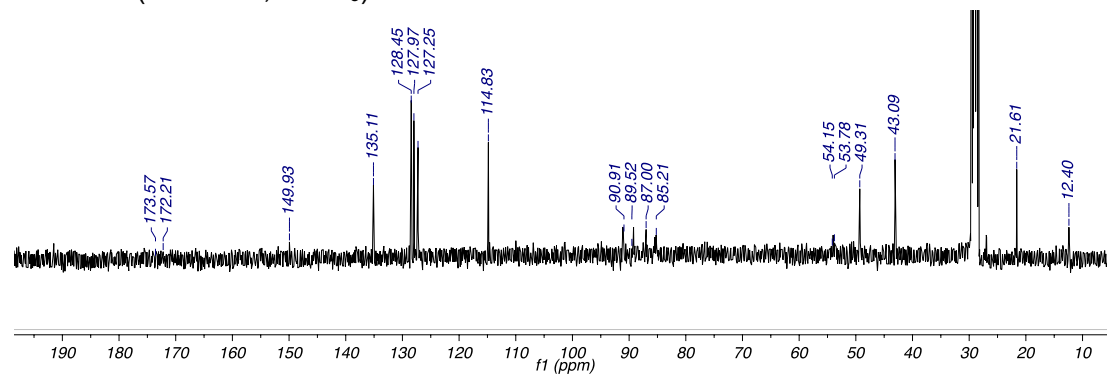


16: 2-(N-allylacetamido)-N-benzyl-2,3,5,6-tetrafluoromethylcyclohexyl)acetamide

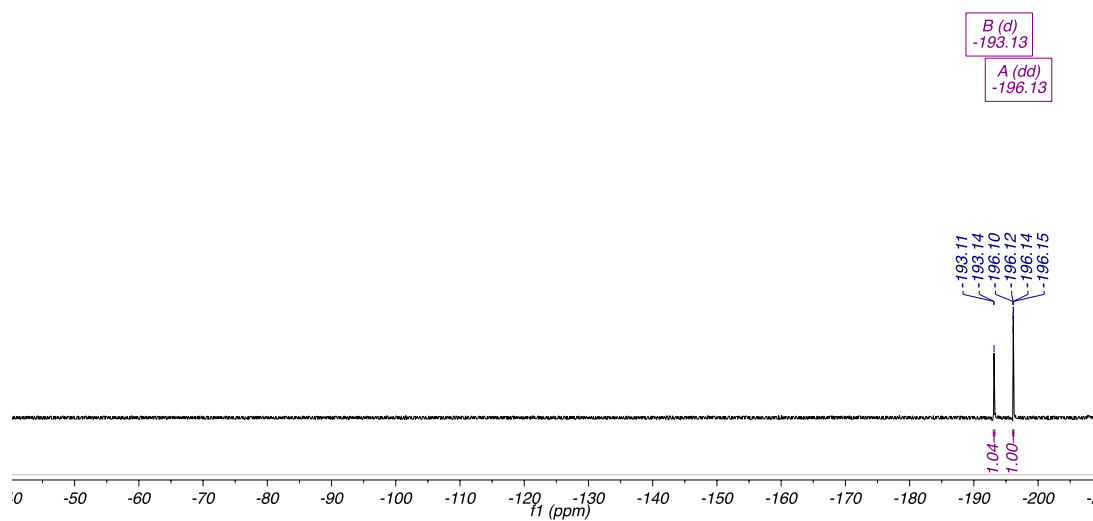
^1H NMR (400 MHz, CDCl_3)



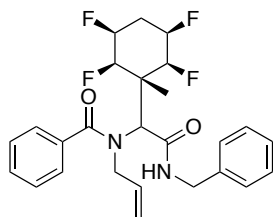
^{13}C NMR (101 MHz, CDCl_3)



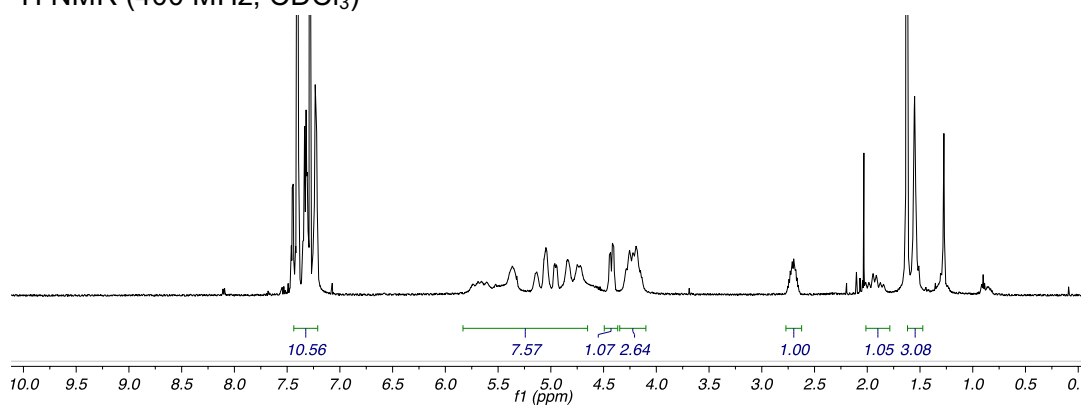
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



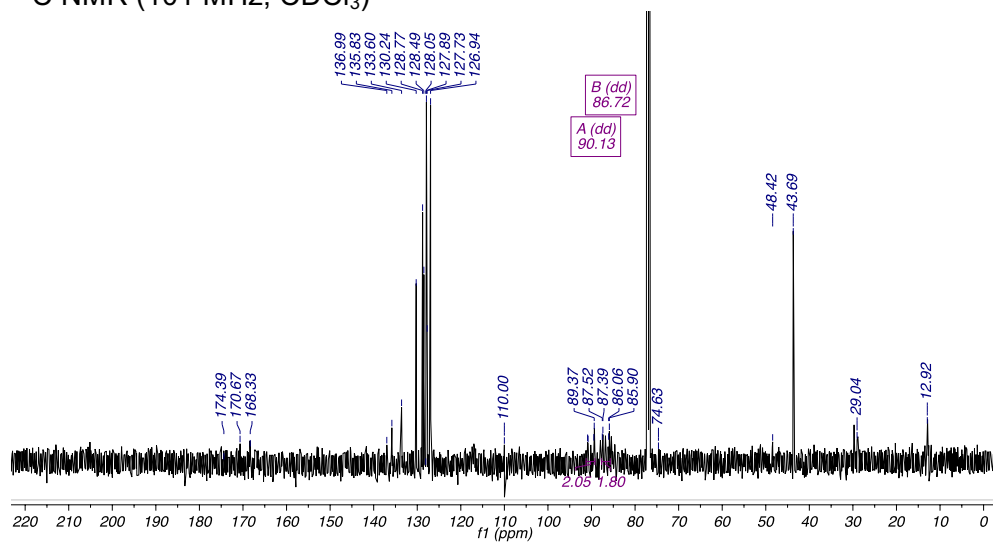
17. *N*-Allyl-*N*-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)benzamide



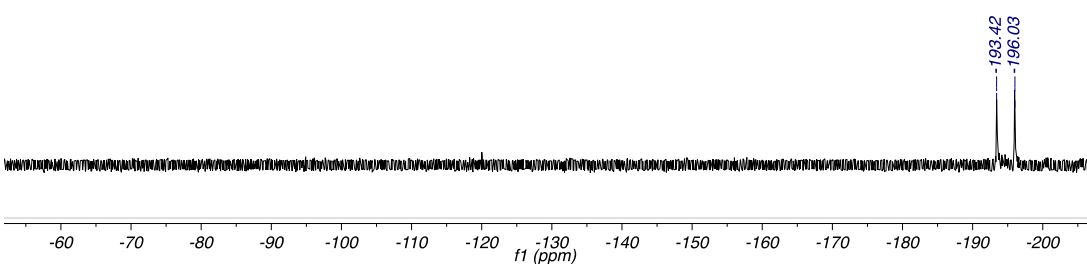
^1H NMR (400 MHz, CDCl_3)

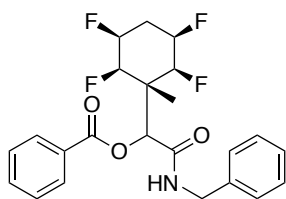


^{13}C NMR (101 MHz, CDCl_3)



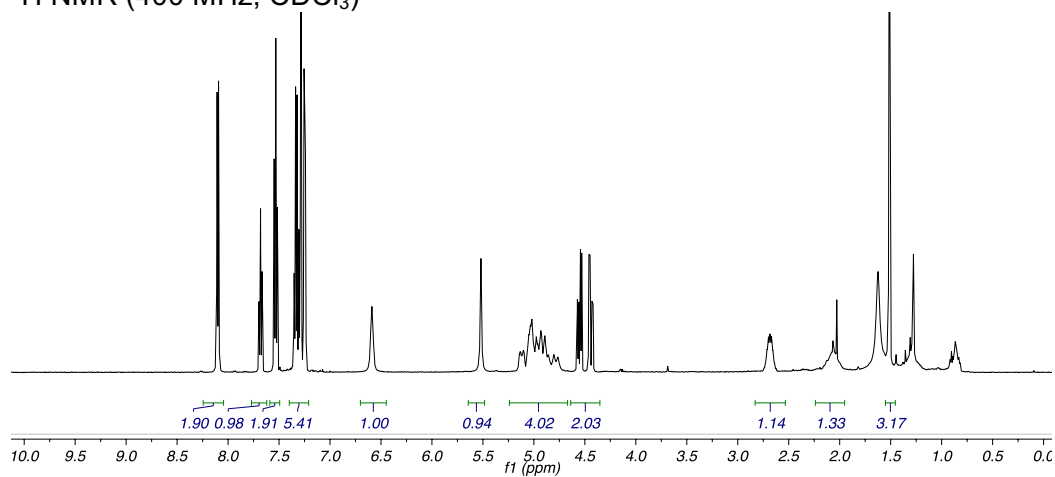
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



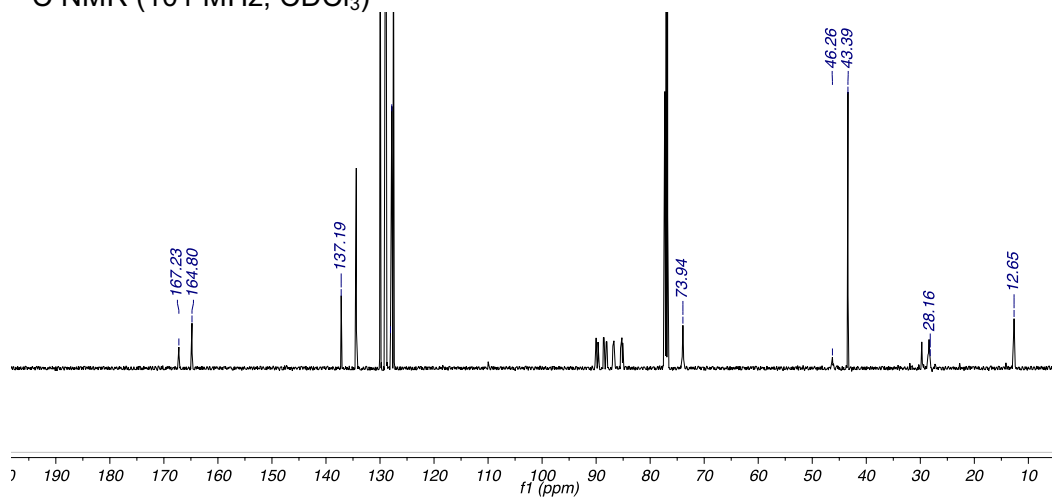


18: 2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexylethyl benzoate

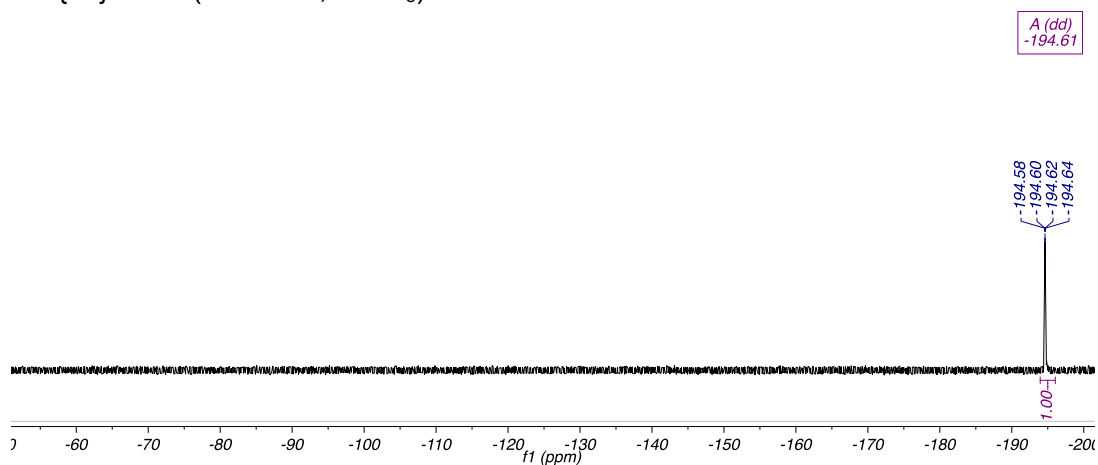
^1H NMR (400 MHz, CDCl_3)

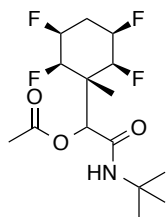


^{13}C NMR (101 MHz, CDCl_3)



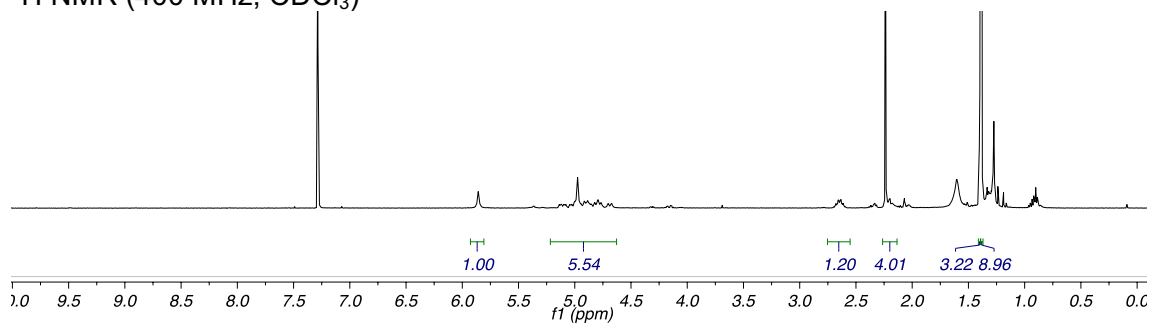
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



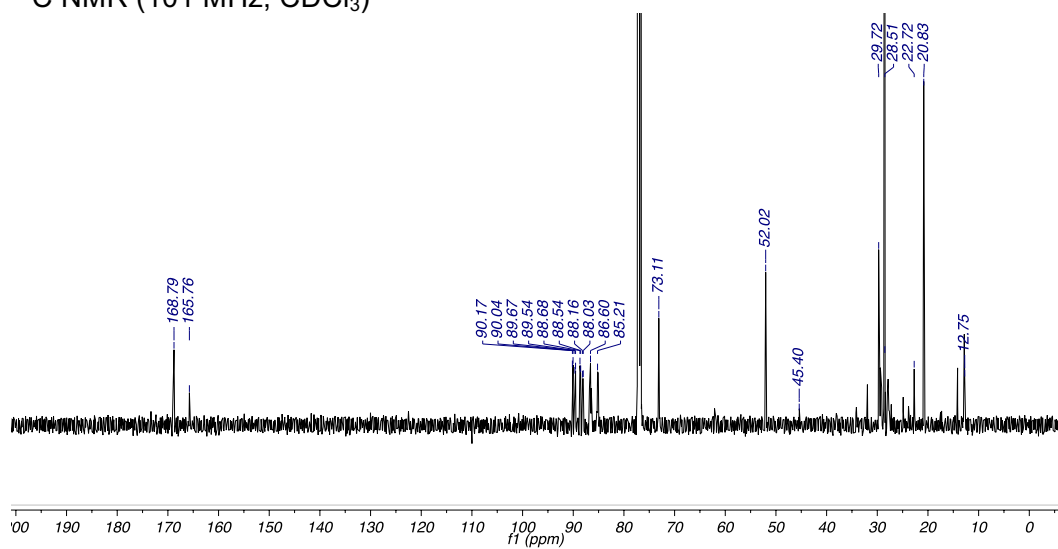


19: 2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexylethyl acetate

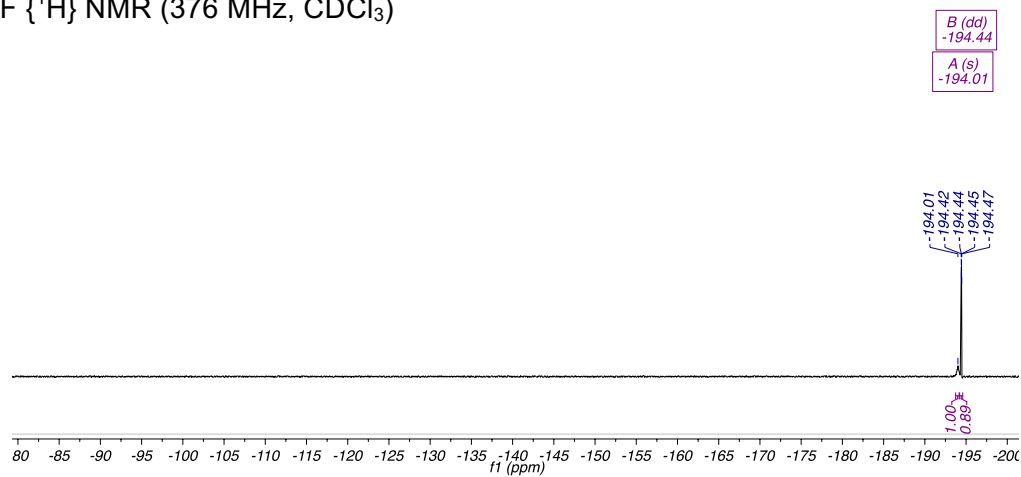
^1H NMR (400 MHz, CDCl_3)

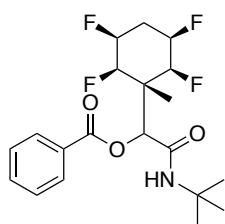


^{13}C NMR (101 MHz, CDCl_3)



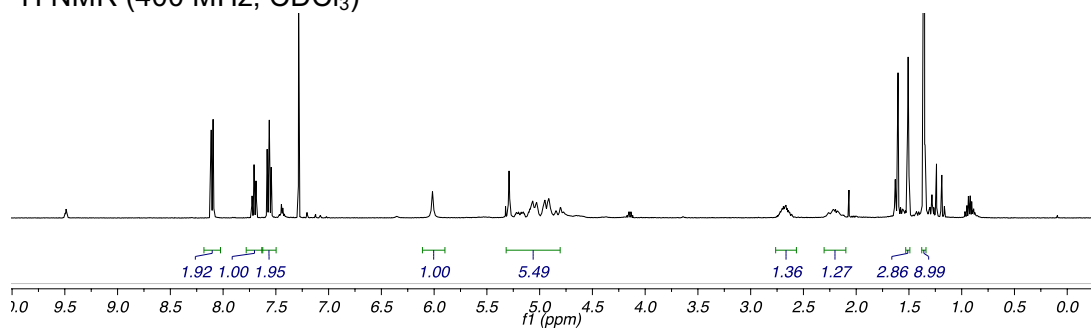
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



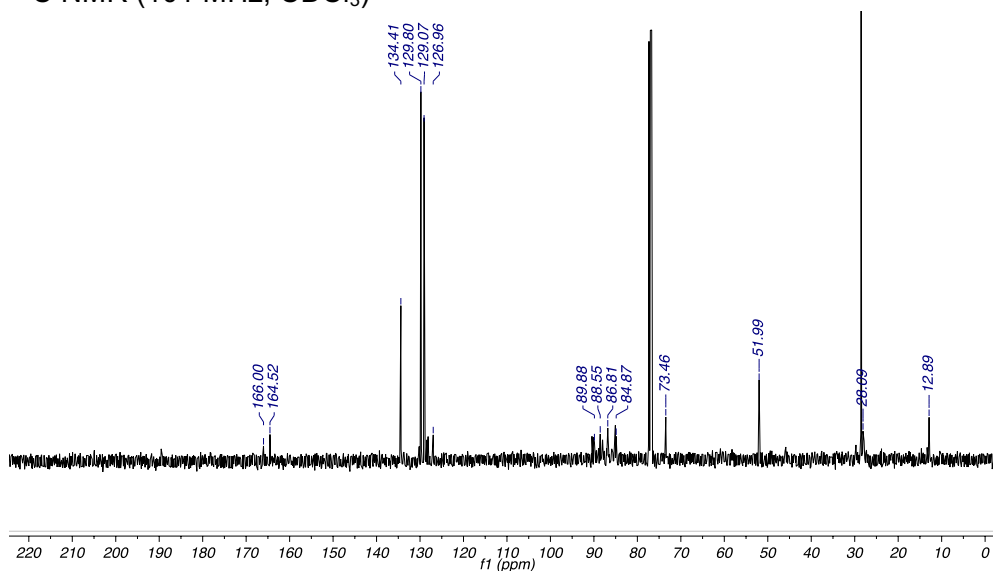


20: 2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl benzoate

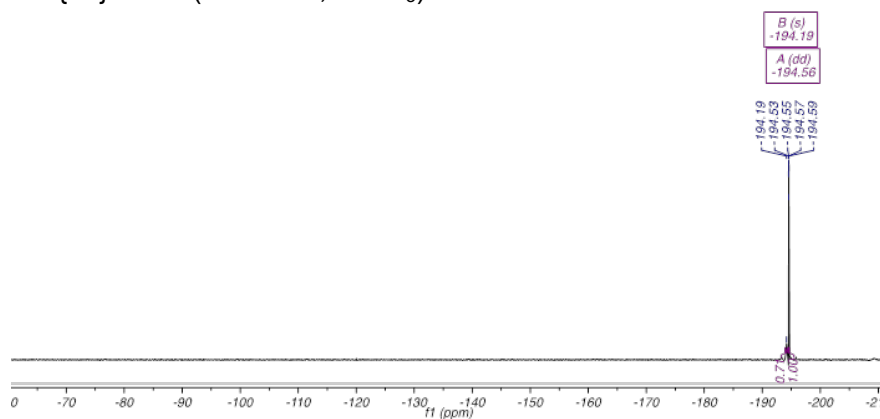
^1H NMR (400 MHz, CDCl_3)

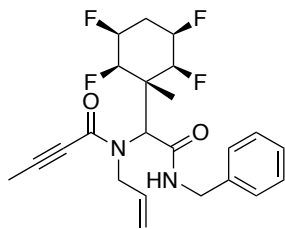


^{13}C NMR (101 MHz, CDCl_3)



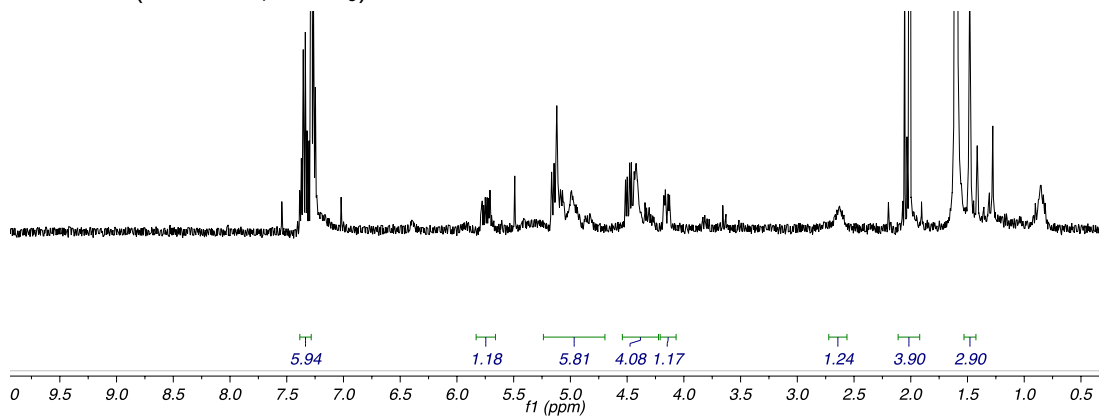
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



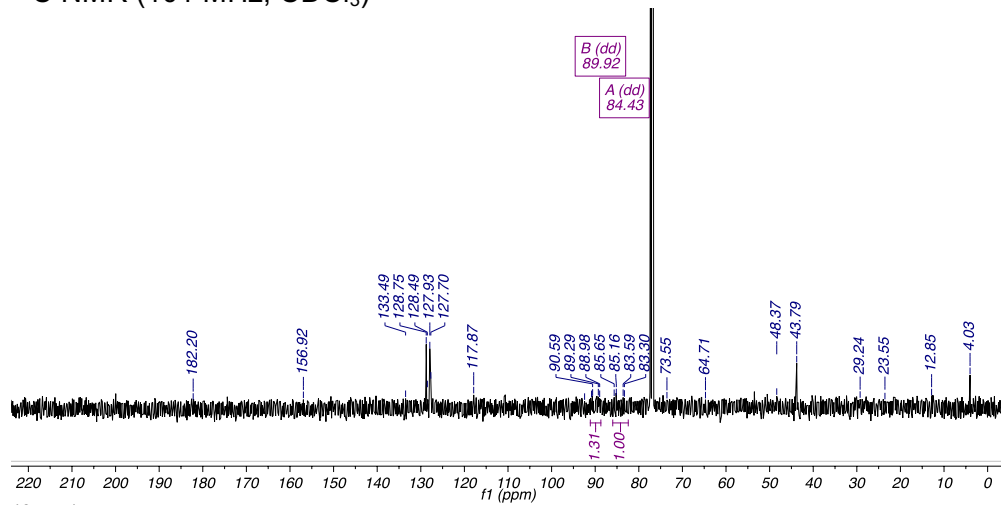


21: N-allyl-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)butynamide

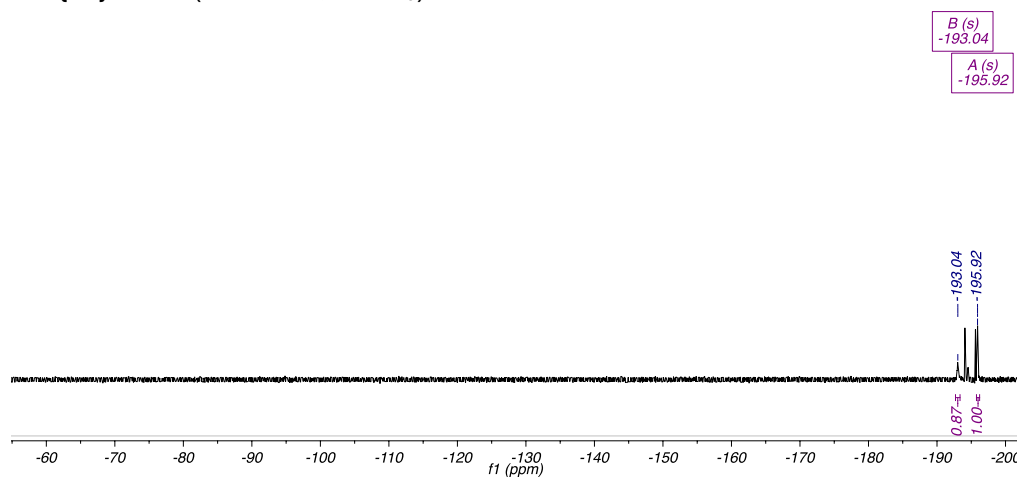
^1H NMR (400 MHz, CDCl_3)

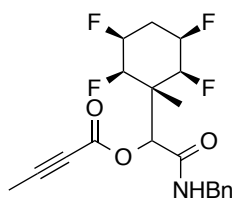


^{13}C NMR (101 MHz, CDCl_3)



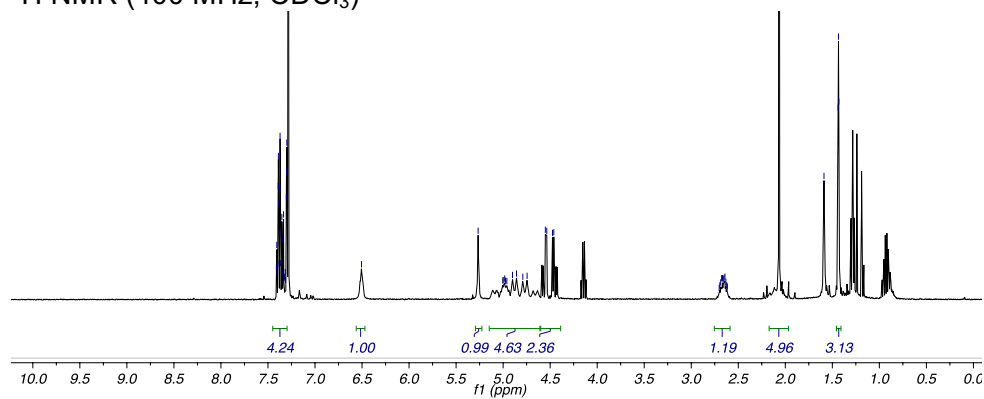
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



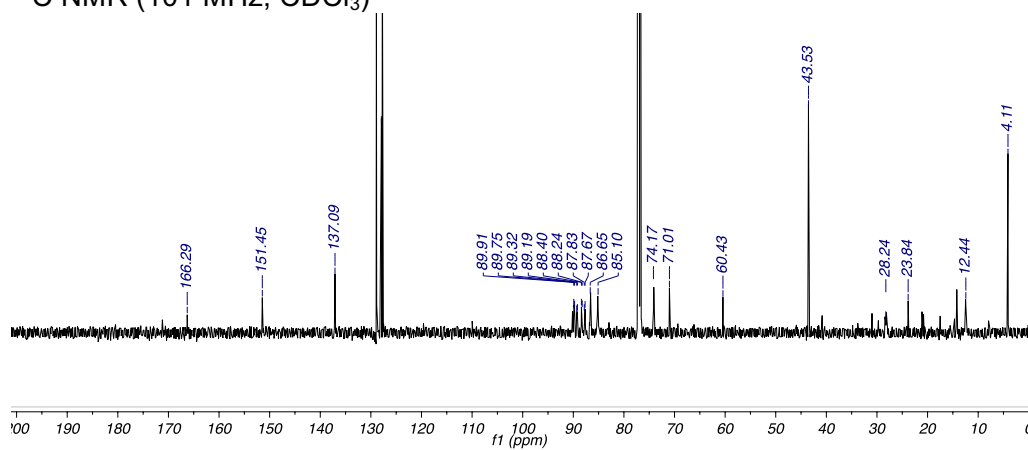


22: 2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl but-2-ynoate

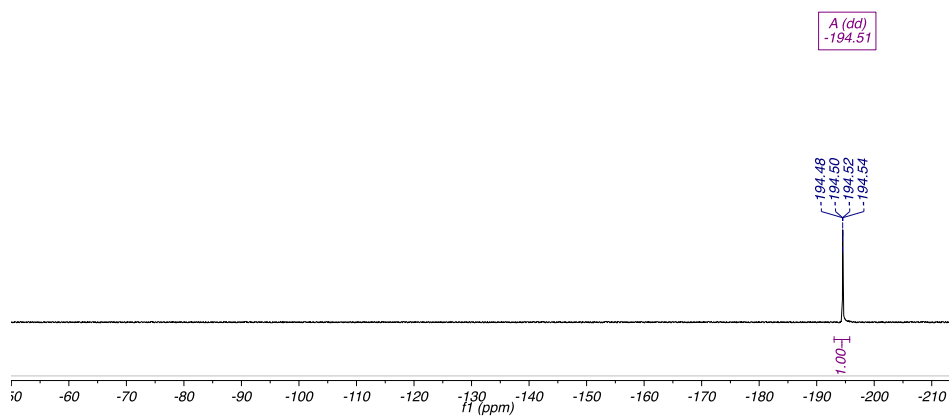
^1H NMR (400 MHz, CDCl_3)

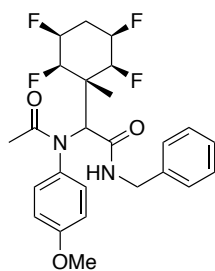


^{13}C NMR (101 MHz, CDCl_3)



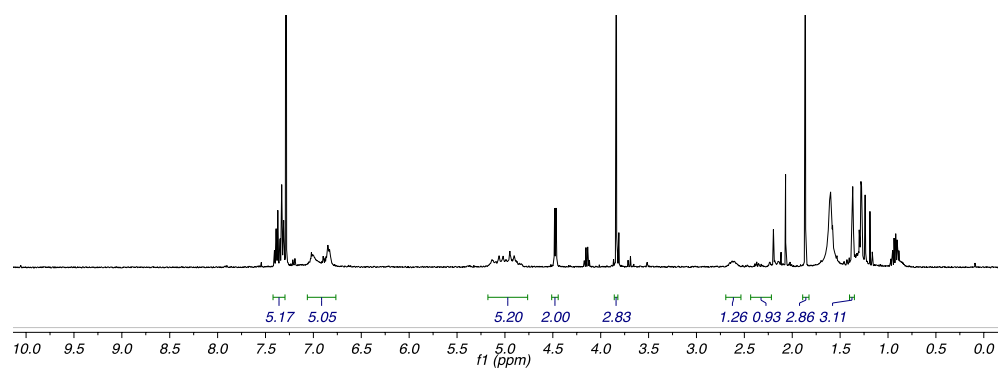
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



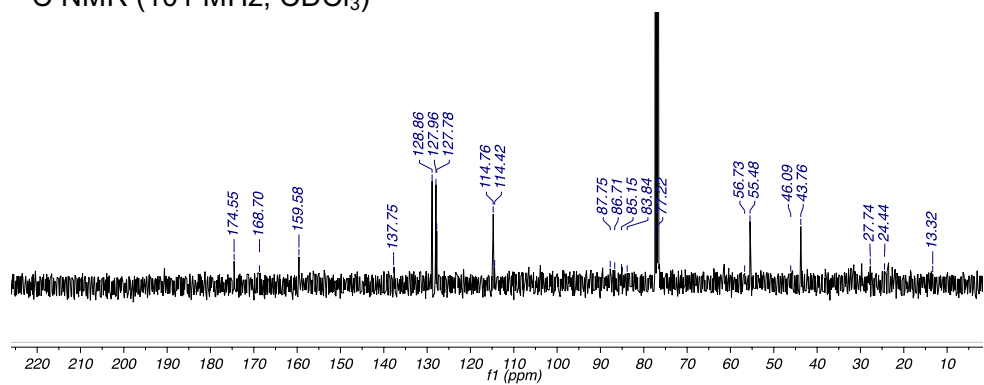


23: Benzyl-2-((4-methoxyphenyl)acetamido)-2,3,5,6-tetrafluoro-1-methylcyclohexyl)acetamide

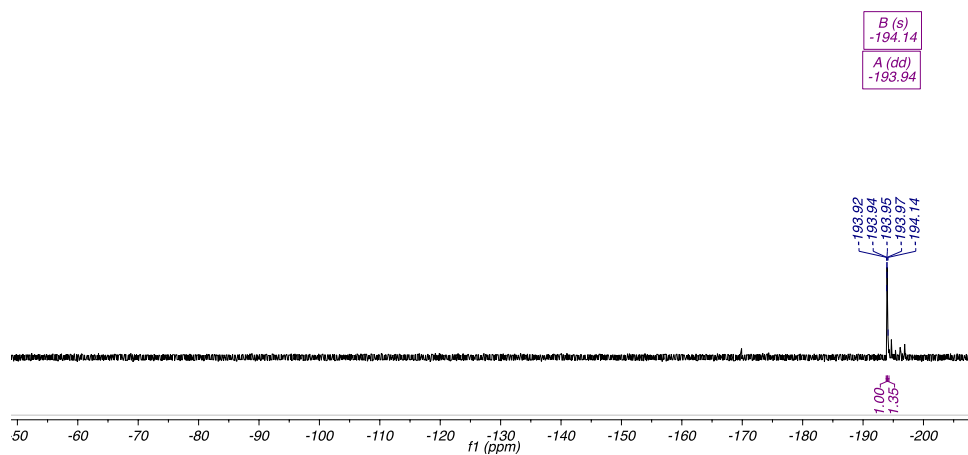
^1H NMR (400 MHz, CDCl_3)

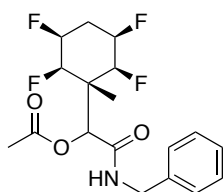


^{13}C NMR (101 MHz, CDCl_3)



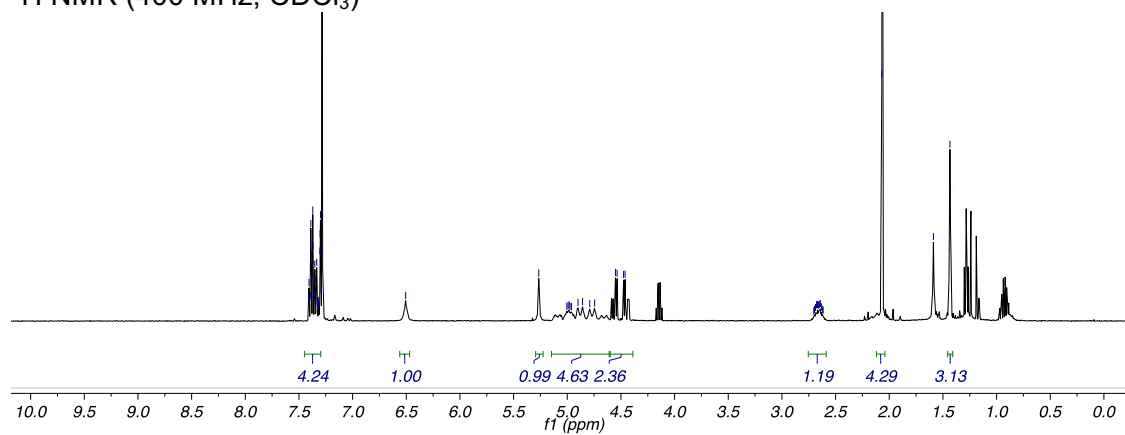
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



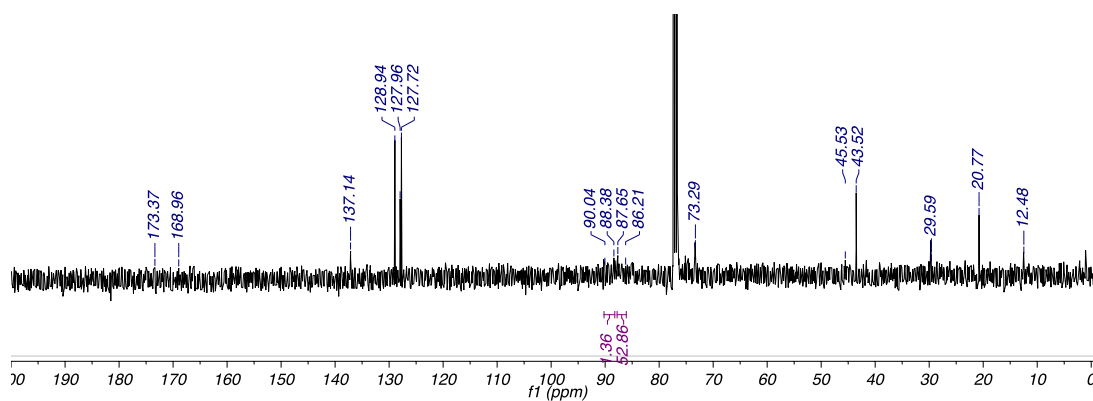


24: 2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl acetate

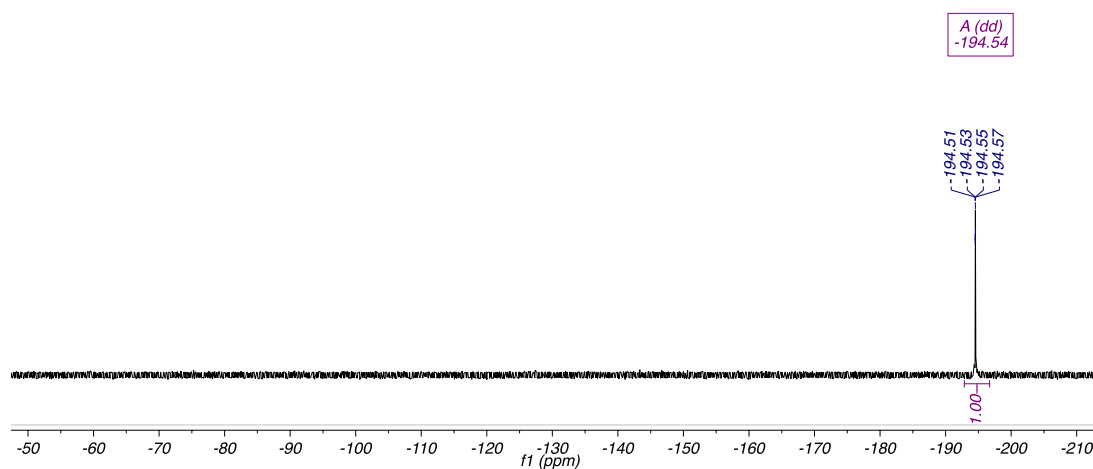
^1H NMR (400 MHz, CDCl_3)

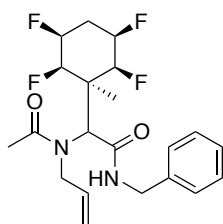


^{13}C NMR (101 MHz, CDCl_3)



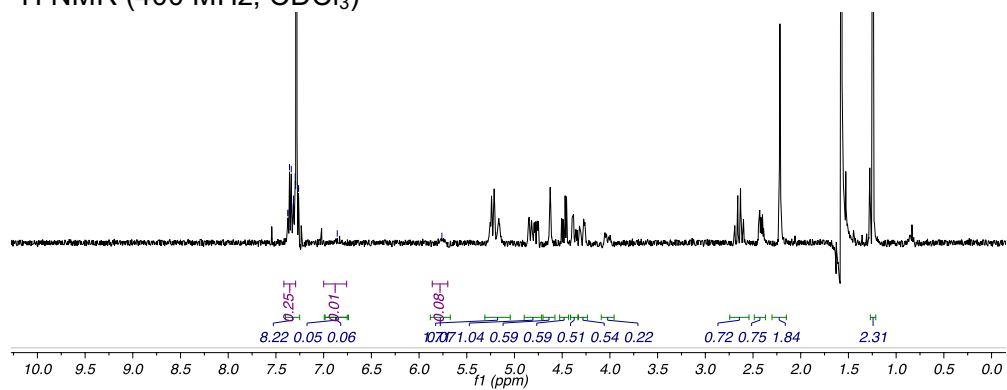
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



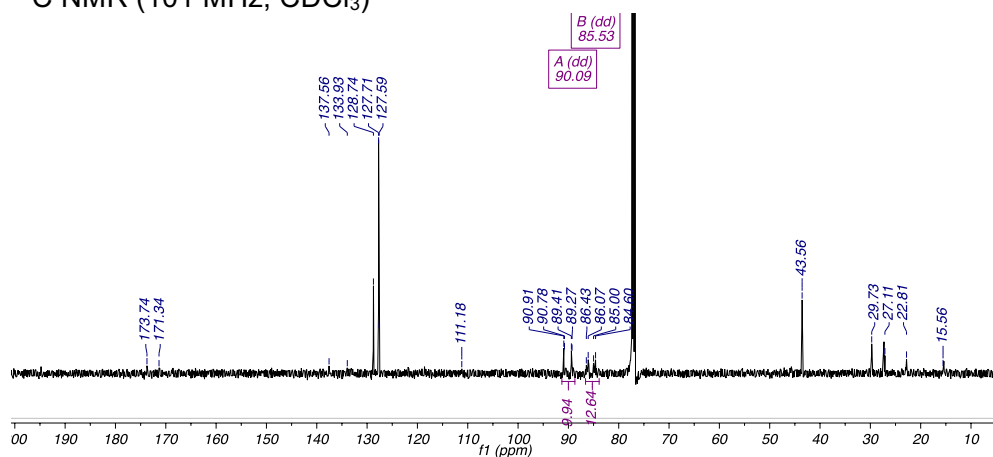


25: 2-(*N*-allylacetamido)-*N*-benzyl-2,3,5,6-tetrafluoro-1-methylcyclohexyl)acetamide

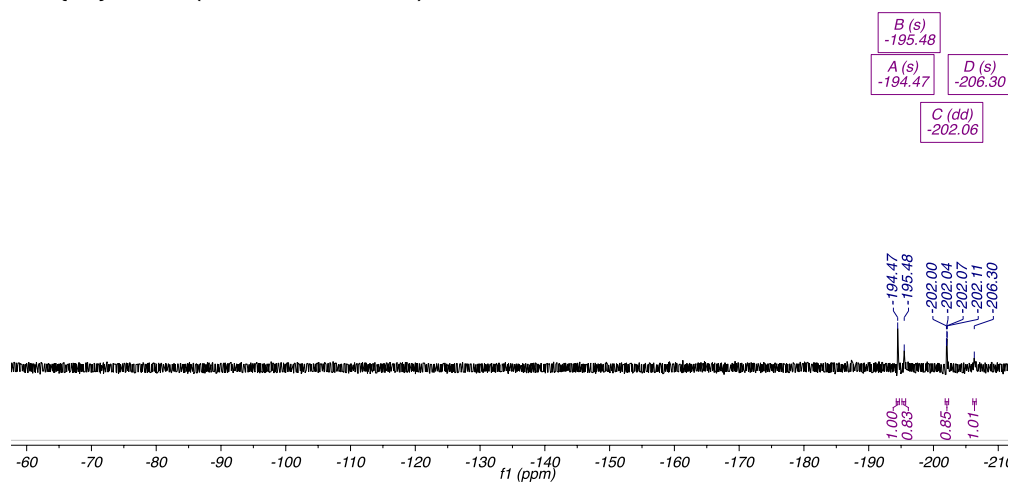
^1H NMR (400 MHz, CDCl_3)

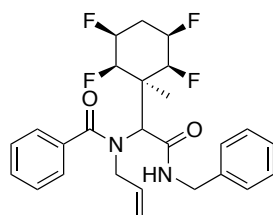


^{13}C NMR (101 MHz, CDCl_3)



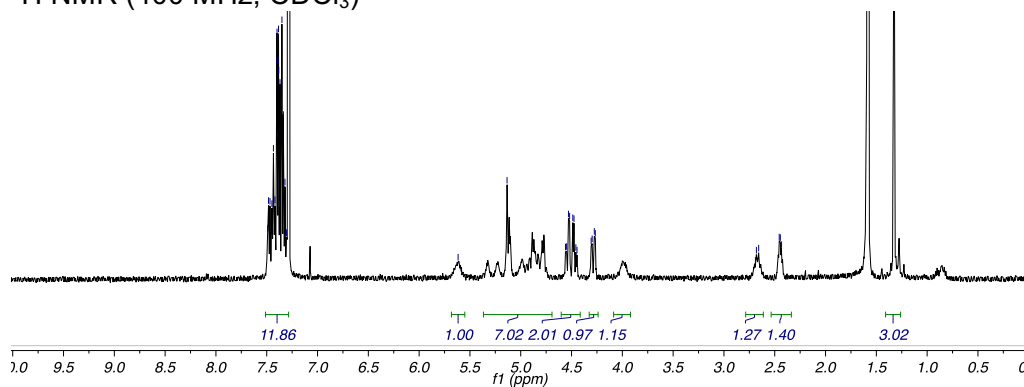
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



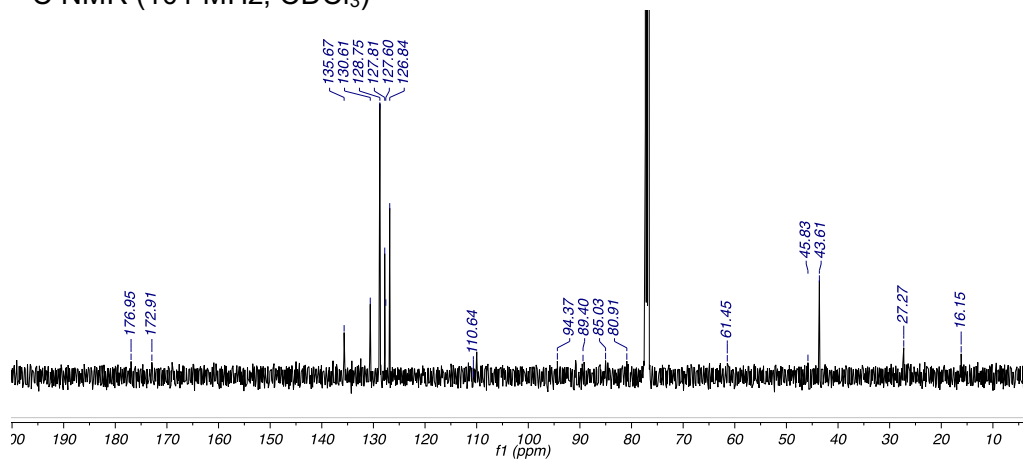


26: *N*-allyl-*N*-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)benzamide

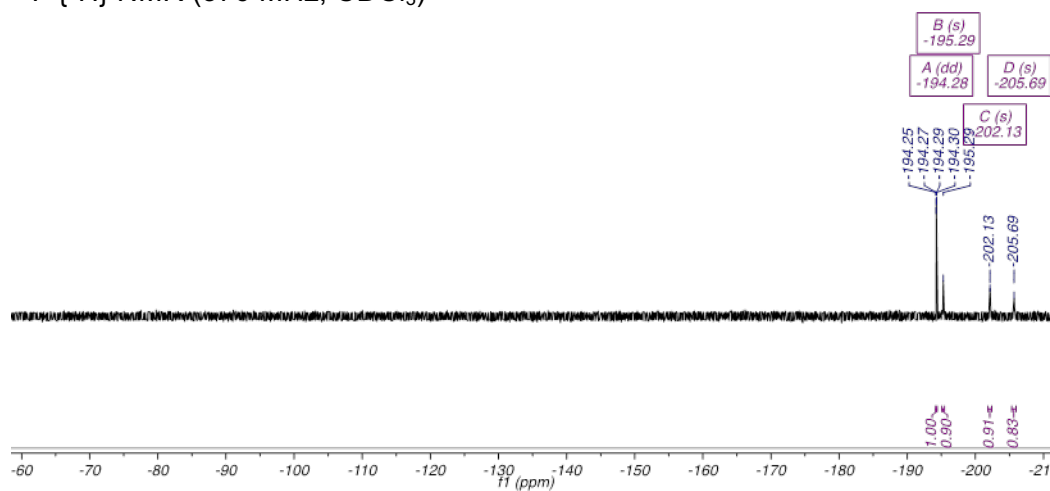
^1H NMR (400 MHz, CDCl_3)

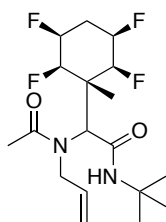


^{13}C NMR (101 MHz, CDCl_3)



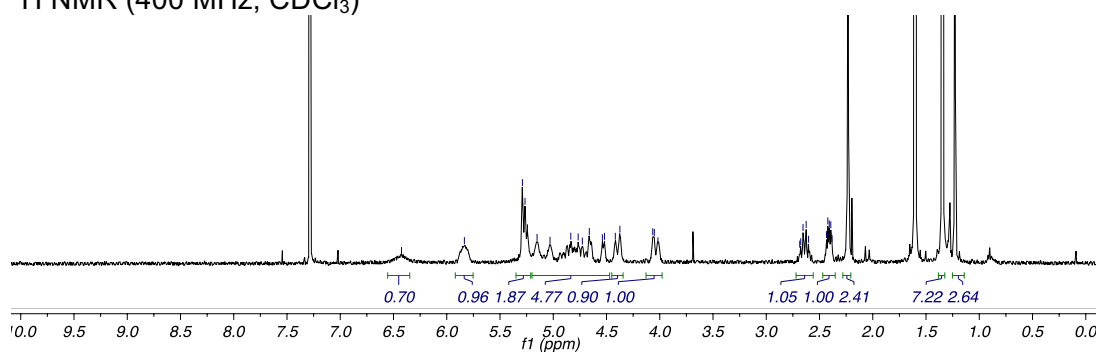
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



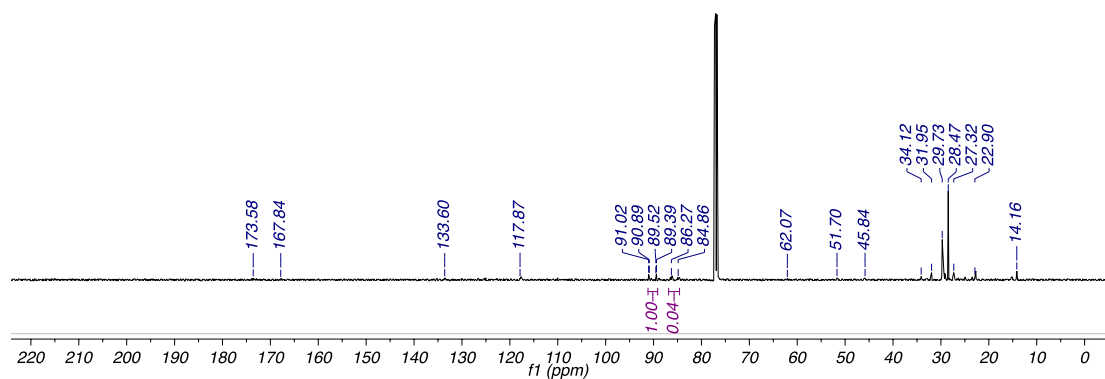


27: 2-(*N*-allylacetamido)-*N*-(*tert*-butyl)-2,3,5,6-tetrafluoro-1-methylcyclohexylacetamide

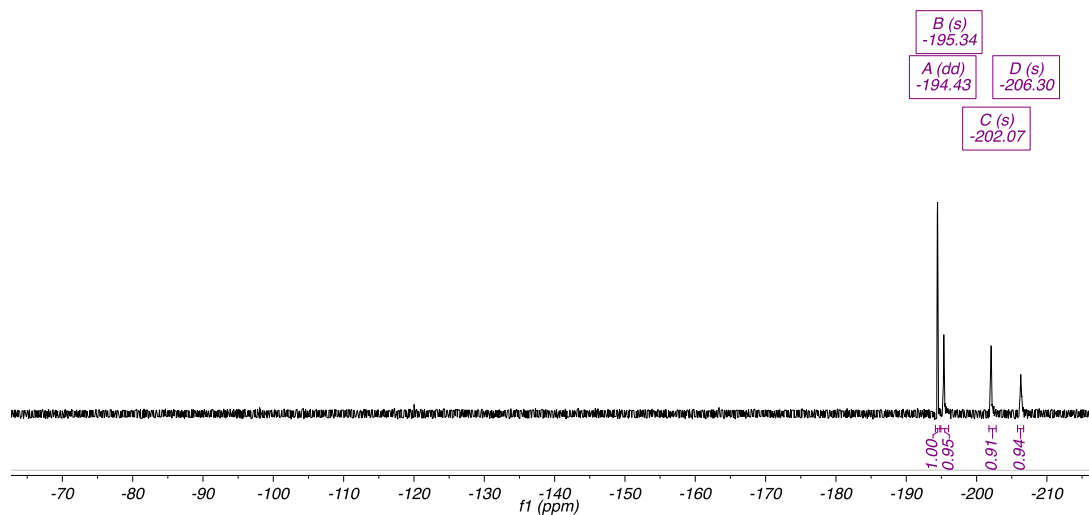
^1H NMR (400 MHz, CDCl_3)

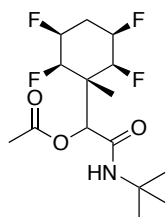


^{13}C NMR (101 MHz, CDCl_3)



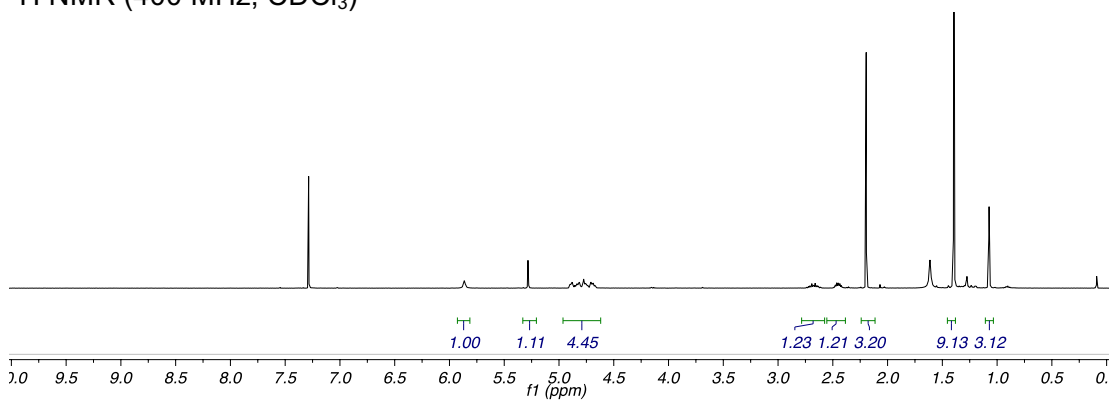
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



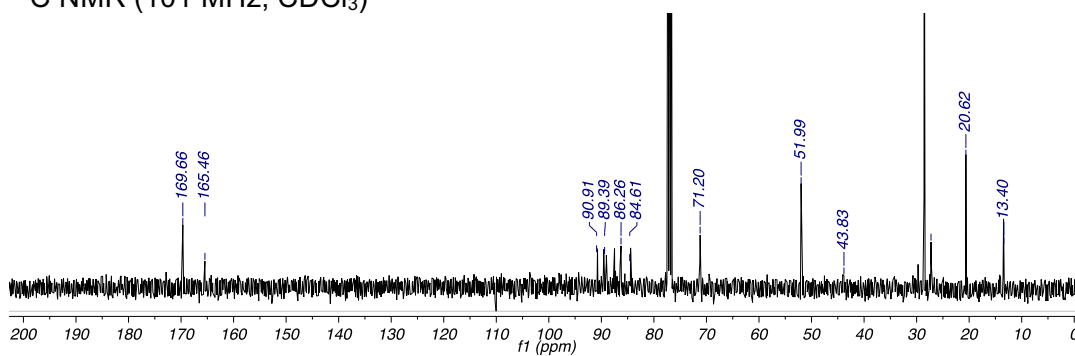


28: 2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl acetate

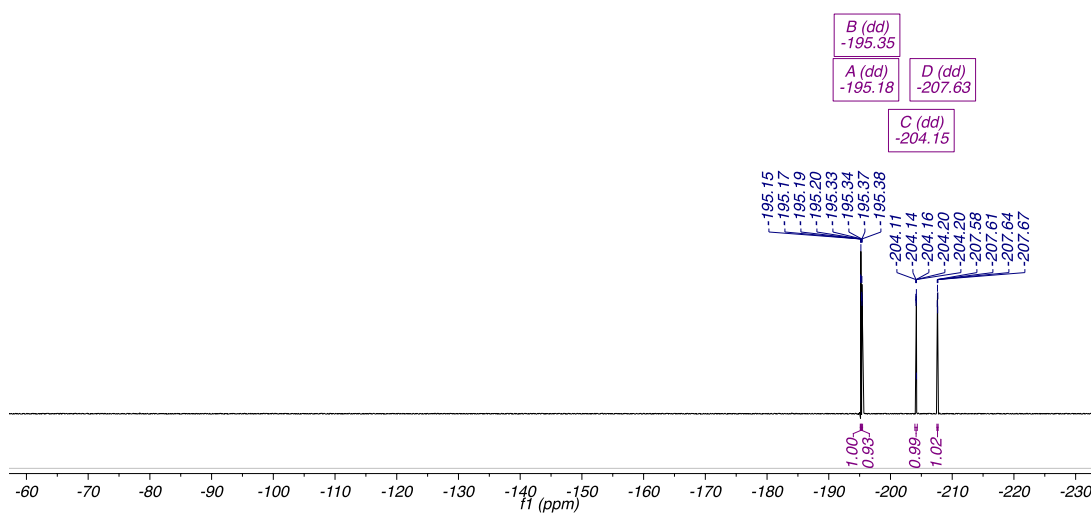
^1H NMR (400 MHz, CDCl_3)

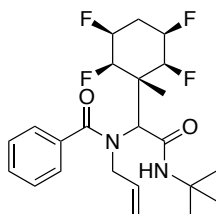


^{13}C NMR (101 MHz, CDCl_3)



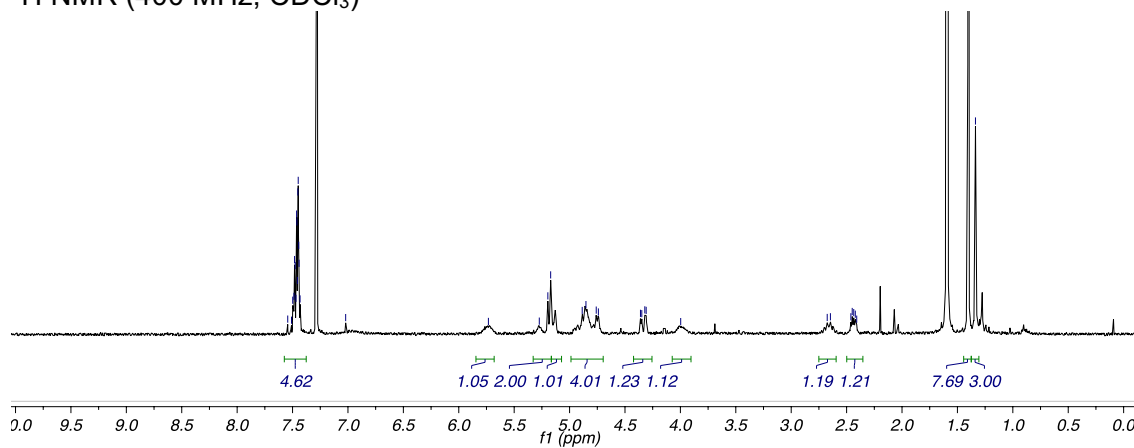
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



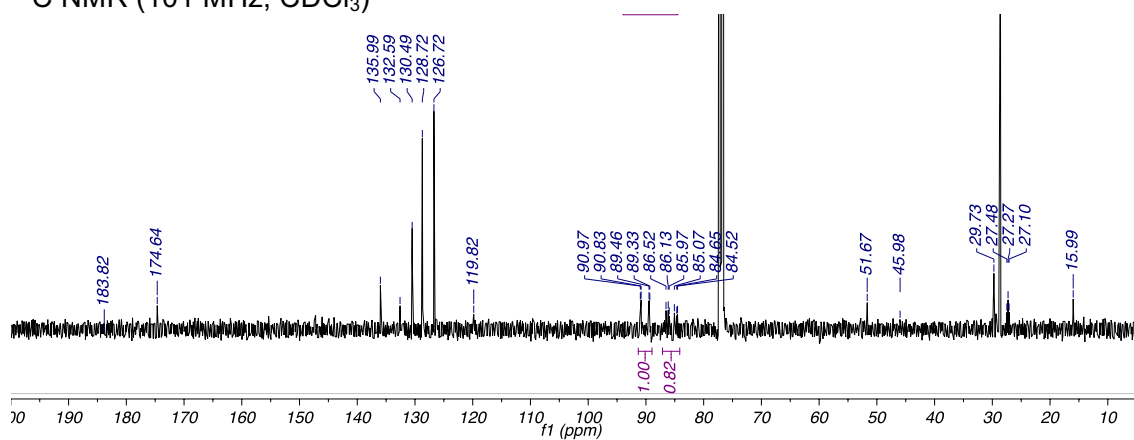


29: *N*-allyl-*N*-2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)benzamide

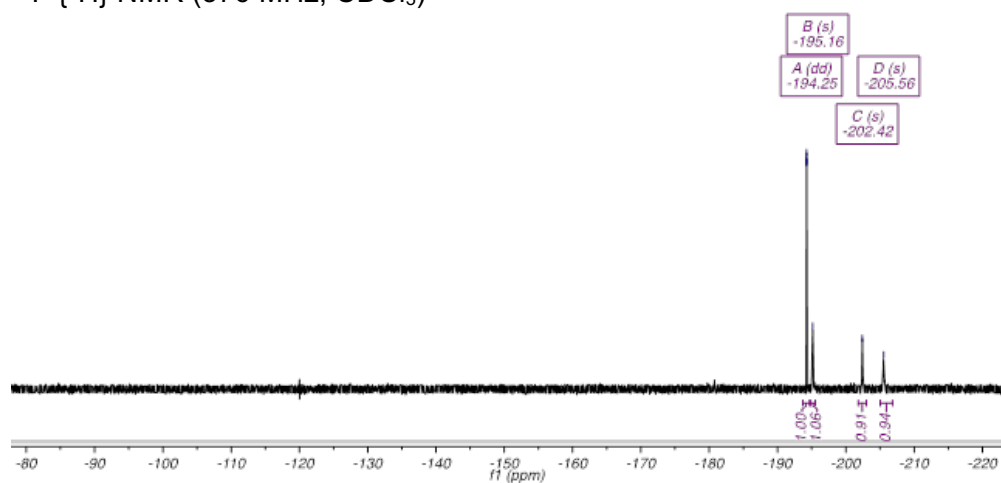
^1H NMR (400 MHz, CDCl_3)

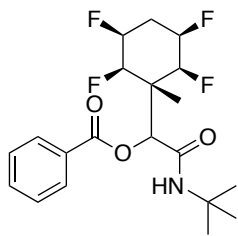


^{13}C NMR (101 MHz, CDCl_3)



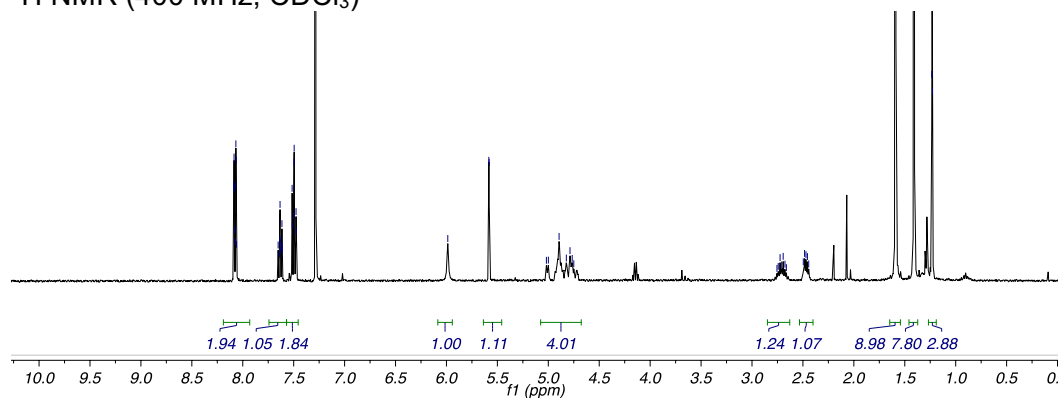
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



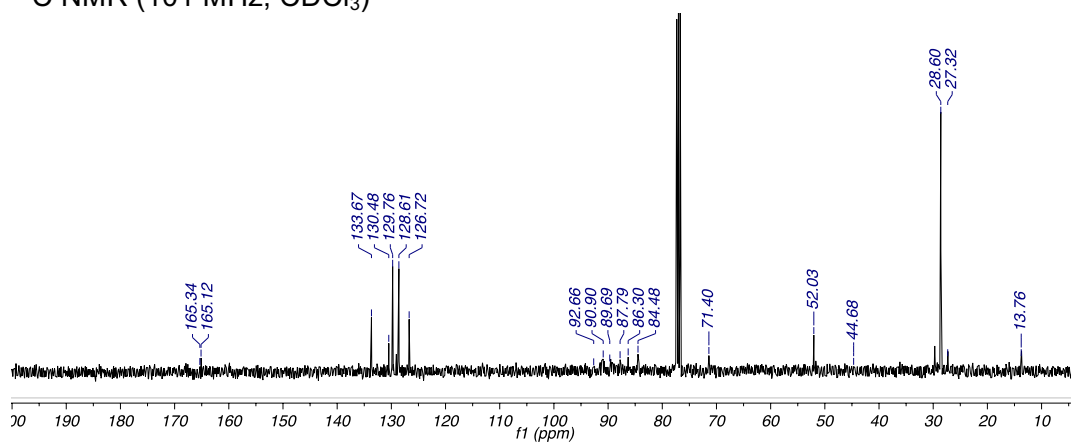


30: 2-(*tert*-butylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl benzoate)

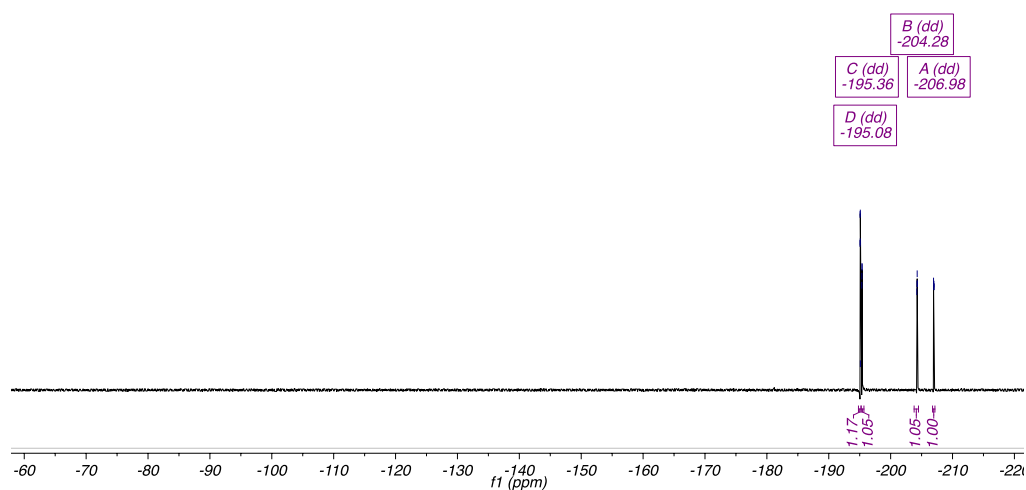
^1H NMR (400 MHz, CDCl_3)

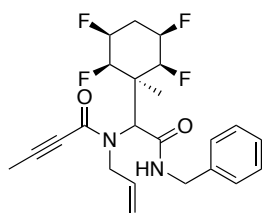


^{13}C NMR (101 MHz, CDCl_3)



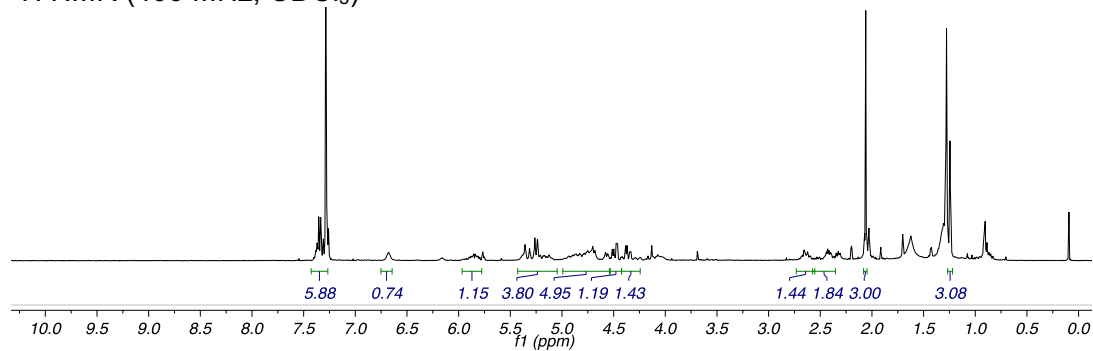
^{19}F { ^1H } NMR (376 MHz, CDCl_3)



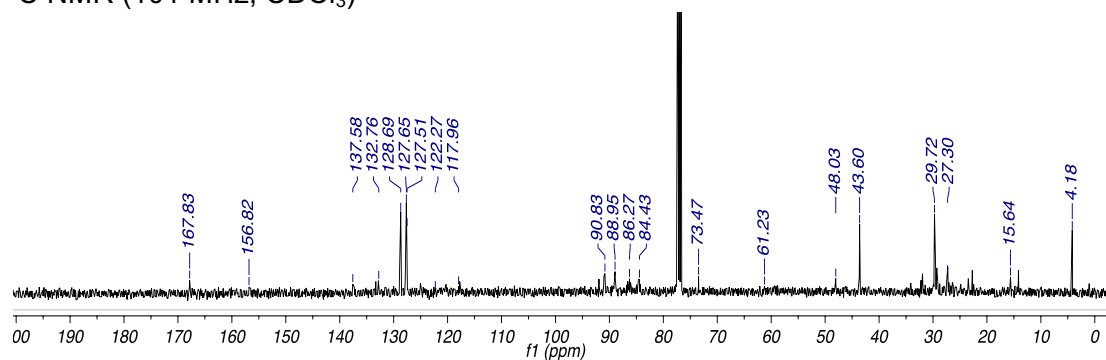


31: *N*-allyl-*N*-2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl)but-2-ynamide

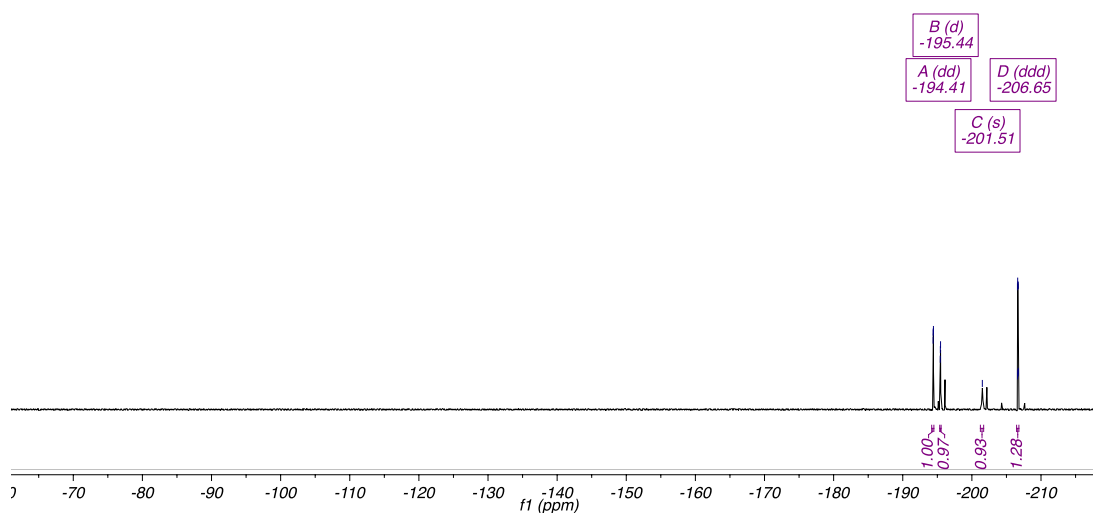
^1H NMR (400 MHz, CDCl_3)

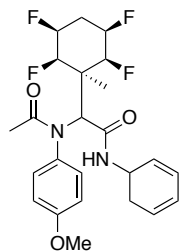


^{13}C NMR (101 MHz, CDCl_3)



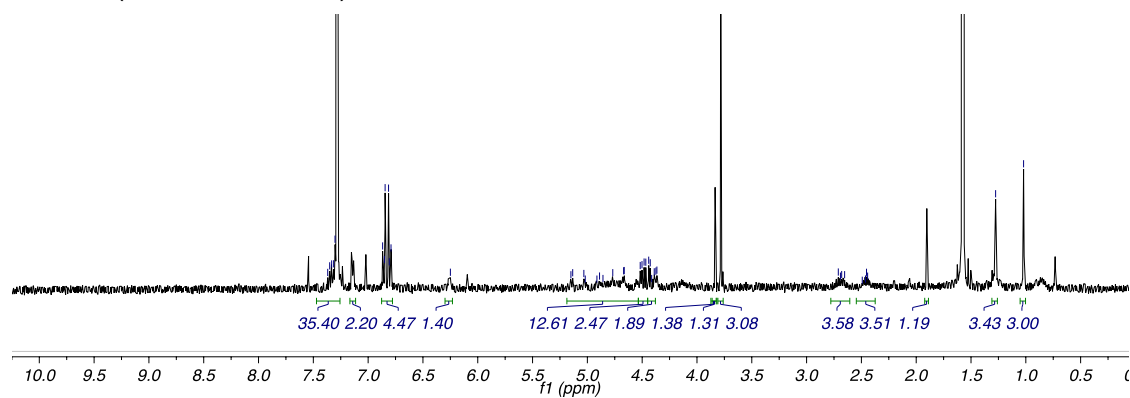
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



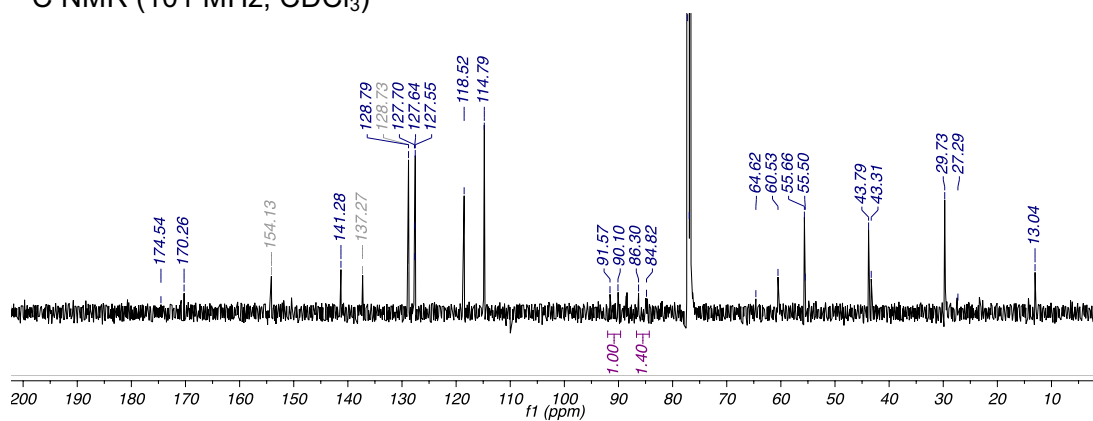


32: N-benzyl-2-(N-(4-methoxyphenyl)acetamido)-2,3,5,6-tetrafluoro-1-methylcyclohexyl)acetamide

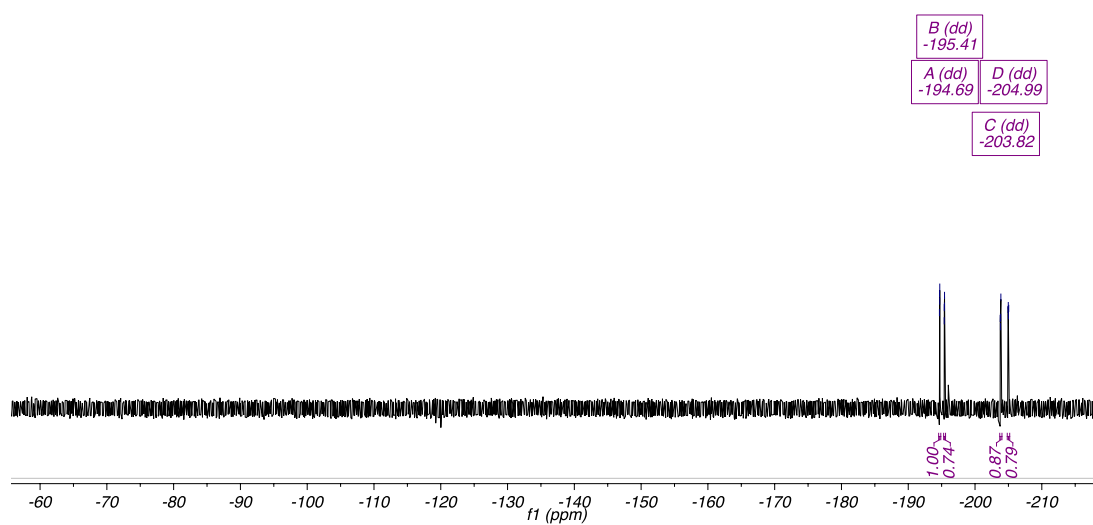
^1H NMR (400 MHz, CDCl_3)

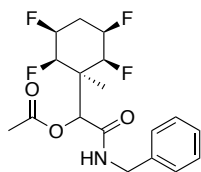


^{13}C NMR (101 MHz, CDCl_3)



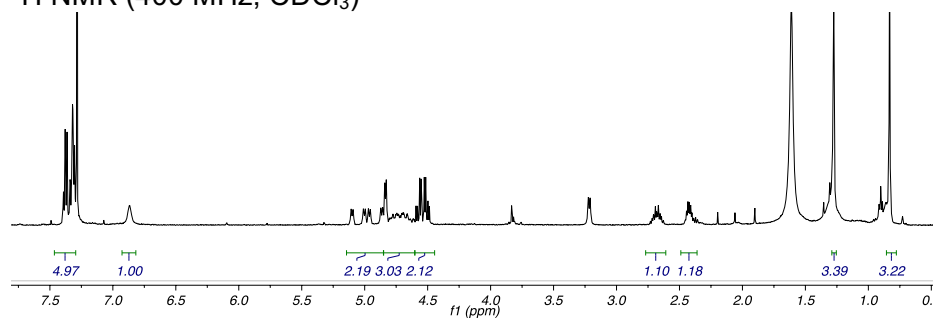
^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)



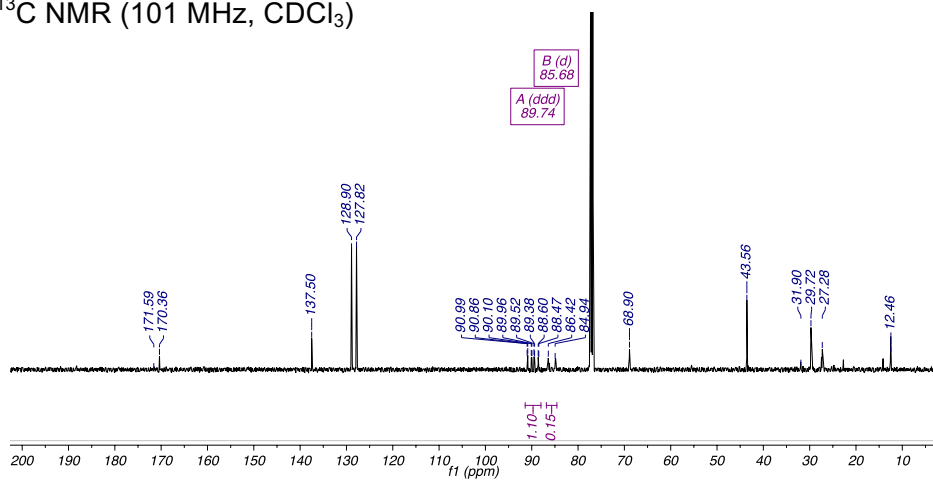


33: 2-(benzylamino)-2-oxo-2,3,5,6-tetrafluoro-1-methylcyclohexyl)ethyl acetate

^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (101 MHz, CDCl_3)



^{19}F $\{^1\text{H}\}$ NMR (376 MHz, CDCl_3)

